

CHEMICAL  
LIBRARY

MAR 2 1948  
JANUARY-FEBRUARY 1948

# THE BULLETIN

OF THE



AMERICAN SOCIETY OF HOSPITAL PHARMACISTS  
VOLUME 5  
NUMBER 1

# A Note from your Editor

This begins a new year for the A.S.H.P. and the fourth year THE BULLETIN has been published in its expanded form. We hope you will find the Society even more of a stimulation to you this year than in the past. We feel certain you will profit from and enjoy this year's Bulletin. Your editors are trying to make your publication one of the best in the field of pharmacy and we know that this volume will surpass the one we brought you last year.

This year we plan to bring you a number of selected articles which have appeared in other journals but which we believe you would like to have readily available in your personal library. We don't know how this plan will work out but we shall make a serious attempt to select material you will want and can use.

For instance, in this issue is a highly important report to the Council on Pharmacy and Chemistry of the A.M.A. regarding organic mercurial germicides, which should be read by every hospital pharmacist. Those on Pharmacy and Therapeutics Committees or on committees to standardize procedures should find it especially valuable.

Then, in looking through Science we found an answer we had been seeking for a long time concerning the results of autoclaving amino acids and glucose in the same solution. Believing you might have been looking for the same answer we have included it on page 26.

Also we saw a description of a method to make projection slides easily, cheaply and rapidly. And we thought there must be a large number of you who teach pharmacology in the Nursing School, or give other lectures, who might be interested in either beginning or enlarging a series of slides for lecture presentation.

Beginning with the next issue, our able Associate Editor Gloria Niemeyer will assume an increasing responsibility with the details of getting THE BULLETIN to press, this together with writing several sections for it. We are fortunate to have an individual like Gloria to do this for us. Since THE BULLETIN began in 1945 she has been contributing in a major way to whatever success it has had and, through it, helping to build a stronger Society. We are also appreciative to the American Pharmaceutical Association for assigning one of its staff members to this

important function which means so much to the members of the A.S.H.P. and to hospital pharmacy as a whole. This is certainly a step in the right direction and Secretary Fischelis is to be congratulated for his foresight and co-operation.

This year the editorial staff will continue to bring you material they believe you will want. The several members of the editorial staff have made notable contributions to the advancement of hospital pharmacy and have served you unselfishly at a personal sacrifice of much leisure time. I know you will all join me in expressing to them our sincere appreciation.

Two new sections are initiated with this issue. In, As The President Sees It, John Zugich will bring you some of the interesting side-lights that go to make the president's job a busy and important one. Herbert Flack will edit, Pharmacy and Public Health. Pharmacy is an important unit of the public health and we believe you will enjoy and profit from this new section which will attempt to show you how pharmacy affects the public health, and vice versa.

Two new members have been named to the editorial staff for 1948. One of them is well known to all of you while the other is a young man relatively new to the field. Mrs. Anna Thiel will be responsible for obtaining descriptions of pharmacy departments for publication. Albert Picchioni will bring you information on newly released drugs and those which will soon be released. He will also note advances in particular fields, as the vitamins, antibiotics, amino acids, and so on. You will want to read the biographical sketches of the new editors on page 38.

We of the editorial staff appreciate fully that we can only furnish you material to develop a better pharmacy service in your individual hospitals. In the final analysis you are the key members of our team, for without your efforts, without your cooperation and interest, and without the basic day-to-day work which only you can do, our efforts are to no avail. To progress, all of us must press forward toward our goal and we not be diverted by the many tangents which daily present themselves.

Cordially,  
Don E. Francke

Chemistry  
Pharmacy  
Direct

## AS The President

3-22-48

57495

Vol 4, no 1-

Chemistry Library

RS

1

A14



## SEES IT

A short time ago, I had some correspondence with Editor Francke regarding a matter which some members of the Executive Committee of the Society felt might be of interest if it were made a part of THE BULLETIN.

The general opinion was that it might be apropos to use some device where background material and sidelights of contemporary Hospital Pharmacy in America, its Society, or its hospital pharmacists could be presented as a kind of "behind the scenes" activity that rarely reaches print. It is hoped that our own personal reader interest for such in hospital, medical and pharmaceutical periodicals will be shared by the readers of THE BULLETIN.

With these thoughts in mind, "As the President Sees It" is borne as an addition to THE BULLETIN with no policy except to intersperse an opinion or two on occasion and to avoid any attempt at gravity.

\*\*\*\*\*

On one week-end during each month, I have the pleasure of taking an excellent train along Long Island Sound to New York for a meeting with Secretary Godley and Treasurer Etheldreda. There are many affairs of the Society that are constantly demanding more attention than correspondence can settle, so that these sessions prove a blessing to get matters activated through leisurely discussion first hand.

Most often our meetings are held either on a Saturday or Sunday lasting from 4 to 6 hours in Brooklyn at Sister Etheldreda's hospital with Secretary Godley making the greatest sacrifice by giving up his tennis courts and a quiet suburban Sunday. The meetings allow for extra thought on current business affairs of the Society and cover such typical agenda as a review of current bills paid, a resume of our financial balance, the progress of committees, correlation of correspondence, relations with the American Pharmaceutical Association, activities of the Division, and general topics which settle internal organizational activities into smoothly functioning projects. From these talks have developed several new procedures within the Society such as a basic budget for 1948; a simplified accounting system that each treasurer can give to his successor without lengthy orientation; election pro-

cedures; quarterly progress reports to all committees and their chairmen of all Society activities; and generally many niceties that an organization that has grown out of the stripling class must indulge in.

During a fine meal that Sister and her hospital always provide us, as typical hospital pharmacists we indulge in "shop talk" concerning the development of our respective departments. Invariably, a pleasant day concludes with Godley phoning Mrs. Godley from Grand Central Station stating that the meeting has ended "much later than anticipated" and to explain to their Sunday dinner guests why he will be 3 hours late.

\*\*\*\*\*

Sometime in the future, I would like to write about the manner in which each issue of THE BULLETIN is "put to bed" by Editor Francke. It was extremely interesting to hear the details for the first time and I am sure the readers cannot visualize them, as I did not, when I viewed the printed page. However, in this the first of the series, I would want to mention just a word about the Editor.

Don E. Francke, along with his office as Chairman in 1944, received the quasi-editorship of the Bulletin which was then issued in mimeograph form. In January of 1945, the first issue of THE BULLETIN appeared in its present format, although not in the slick paper variety nor yet subjected to constantly spiralling printing costs.

Editor Francke as a hospital pharmacist knew what other hospital pharmacists wanted and sent out the first issue with some trepidation not knowing whether his opinion would be accepted. Fortunately, the response was gratifying so that he neatly promoted himself into a voluntary, non-compensatory 16 hour day. Due to the nature of the printing process, he had to acquire the abilities of an artist, managing editor, researcher, paper expiditer, photographer and above all a perfect typist as his pages were photographed and printed from that copy. During his editorship, he still maintained one of the finest hospital pharmacy internship programs, training several at a single time, published a formulary that is a text in scope, found time to give talks to spur hospital pharmacists on at many distant

02.4



points, speak on a national radio network on hospital pharmacy, continue studies toward a higher degree—all in stride with his responsibility of being chief pharmacist of a 1000 bed institution.

To no single man is a greater debt owed by the American Society of Hospital Pharmacists. Through his efforts and leadership at much personal sacrifice, his Bulletin has been a periodical that is unparalleled—without any full-time staff nor advertising to assist in overcoming budget limitations. Its pages have filled a void in information and provided many hospital pharmacists with practical suggestions and inspiration for development in their own bailiwick. One cannot help but salute this quiet mannered, unassuming hospital pharmacist who is a bear for work and pregnant with ideas which benefit hospital pharmacy. Men like Don E. Francke come to organizations once in a decade.

\*\*\*\*\*

On the back page of each Bulletin, there usually appears a photograph captioned "American Institute of Pharmacy." For those hospital pharmacists who have not had the opportunity to visit Washington let me say that any photograph can do little justice to the building. Set back on a spacious lawn it overlooks a broad boulevard, parks and the Lincoln Memorial. Beyond the red leather panelled entrance, the activity within belies its serene exterior.

When ushered in by the receptionist and you become seated in a spacious rotunda, a museum with its pharmaceutical curios can be seen on the left and the library with its gleaming study tables on the right. The first floor is occupied by offices of the editorial and secretarial staff of the American Pharmaceutical Association. In the far end of the hall is the office of Dr. Fischelis, with its telephones, desks and tables stacked high with correspondence and reference material so that one wonders how one man can possibly handle the vast responsibility that is his. The remainder of the first floor is occupied by conference rooms executed in excellent architectural taste. The lower floor is occupied by the N.F. research laboratory busy in its current problems under the jurisdiction of Dr. Powers and Dr. Green.

To the public, the building's location and architectural style can be summed up in one word—Dignity. To all pharmacists, it should be a pride as the "front room" in the heart of the nation's affairs, for American Pharmacy. I am sure hospital pharmacists too, will share that pride even more when the full time Director of the Division of Hospital Pharmacy will be centered there.

\*\*\*\*\*

Sometime in discharging the responsibility as President, one becomes enmeshed in unforeseen circumstances. A short time ago, I was asked by the Chairman Dondero of the Massachusetts Society of Hospital Pharmacists to address that regional affiliate. Somehow our letters and telephone conversation became garbled as to the meeting place. Since I was to have someone meet me at the train I was not concerned, until coming into Boston, my country naiveness discovered that rather than a Union Station the city had two stations—"North" and "South." With no one meeting my train after I waited a half hour, I decided that activity was called for. I tried to make telephone contacts to no avail. At the information booth I did the best with an individual next to me who had an epileptic seizure. I had the public address systems at both stations indistinctly calling Mr. Barry the local Society's greeter. Finally calling his hospital in Worcester, I learned that the meeting was 45 minutes by train, in that city. Catching the next train to "Wuster" (not Wooster-Westerners) I hurriedly took a taxicab to the meeting at the St. Vincent Hospital auditorium arriving in the final five minutes of the session. It all ended with a fine note when we had our informal pleasantries over tea and an open forum meeting, but in the role of President my platform manner was not enhanced by the panting delivery.

Cordially,

*J. Zugich*





VOLUME 5 - NUMBER 1

JANUARY-FEBRUARY 1948

DON E. FRANCKE  
Editor

GLORIA F. NIEMEYER  
Associate Editor

#### ASSISTANT EDITORS

Paul F. Cole  
Sister Mary Etheldreda  
Herbert L. Flack  
Leo F. Godley  
Albert P. Lauve  
George L. Phillips  
Albert L. Picchioni  
Evlyn Gray Scott  
Anna D. Thiel  
Eddie Wolfe

Publication Office  
and  
Editorial Office  
at  
University Hospital  
Ann Arbor  
Michigan

Copyright 1948 by the  
American Society of  
Hospital Pharmacists

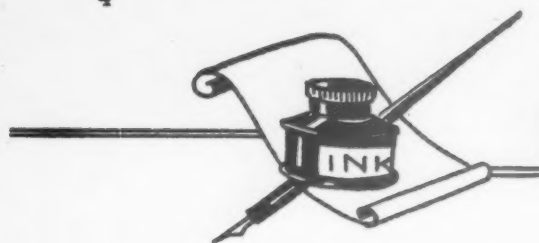
THE BULLETIN is published bimonthly by the American Society of Hospital Pharmacists, a national organization devoted to the profession of hospital pharmacy, dedicated to the interests of the hospital pharmacist, and pledged to cooperate with the American Pharmaceutical Association with which it is affiliated.

Contributions of articles by hospital pharmacists, or by others interested in the progress of this important branch of the public health profession, will be accepted if they are of general interest to those in hospital pharmacy. The editors reserve the right to revise all material submitted, if necessary.

The American Society of Hospital Pharmacists and the American Pharmaceutical Association assume no responsibility for the statements and opinions advanced by contributors to THE BULLETIN. Views expressed in the editorials are those of the editor and do not necessarily represent the official position of the American Society of Hospital Pharmacists.

#### CONTENTS

As The President Sees It . . . . .	1
Correspondence . . . . .	4
What The Hospital Pharmacist Wants, An Editorial . . . . .	5
Therapeutics Committee And The Hospital Formulary . . . . . Don E. Francke	6
Ampuls . . . . . Leonard Yoder, Eunice Anderson Royer and H. Geo. DeKay	14
New Members . . . . .	19
The Bacteriostatic And Bactericidal Actions Of Some Mercurial Compounds On Hemolytic Streptococci . . . . . Harry E. Morton, Leon L. North, Jr. and Frank B. Engley	20
Inactivation of Nutrients By Heating With Glucose . . . . . A. R. Patton and E. G. Hill	26
Therapeutic Trends . . . . .	27
Timely Drugs . . . . .	29
Pharmacy And Public Health . . . . .	31
Answers To Queries . . . . .	33
Notes And Suggestions . . . . .	35
A Method For Making Lantern Slides . . . . . Hans Neuberger	36
What's News About The Antibiotics . . . . .	37
The Veterans Administration Pharmacist . . . . .	39
Southeastern Hospital Pharmacy Association Semi-Annual Meeting . . . . . Joe Vance	42
Current Literature . . . . .	44
Organization News . . . . .	45
News Items . . . . .	47
Positions In Hospital Pharmacy . . . . .	48



## CORRESPONDENCE

Dear Sirs: In connection with our survey of the hospitals of Indiana it has become evident that we should have a set of standards for the equipment and operation of a hospital pharmacy much as we have standards for accredited schools of pharmacy. Undoubtedly it would be necessary to establish different sets of standards for small and large hospitals. Possibly your organization has done something along this line. If it has not, it might be well to establish a committee on standards for hospital pharmacy. What I have in mind is that in the inspection of hospital pharmacies, which run all the way from a drug cabinet used by a nurse to a pharmacy with one or more pharmacists in charge, we have no yardstick against which to measure them. If we had a set of standards to call to their attention, it would be very probable that we could secure cooperation in improving the service rendered in our hospitals in the various states. Furthermore, boards of health, hospital administrators, and others would begin to consider their setup in comparison with the standards and eventually great good could be brought about. Eventually there might even be a system of accreditation of hospital pharmacies, but that would be something in the nature of a long range program. I am simply sending on this general idea in the hopes that your organization may find it possible to make a beginning by studying the matter.

Glenn L. Jenkins, Dean

School of Pharmacy  
Purdue University

Dear Sirs: I wish to express my approval of the Division of Hospital Pharmacy within the American Pharmaceutical Association which I feel is an advancement in the recognition due the American Society of Hospital Pharmacists. I wish also to express my thanks to those who worked so hard to bring about this recognition.

Thomas E. Sisk

St. Joseph Hospital  
Lorain, Ohio

Dear Sirs: We have been talking about extending the work of the Hospital Pharmacists in Texas

and as an immediate project we are trying to arrange to have one hospital pharmacist appointed to the Texas State Board of Pharmacy. Would you please check the attached list of A.S.H.P. members which was taken from THE BULLETIN. We want to make sure that we have all the Texas members listed.

Edward W. Brady

Dallas, Texas

Dear Sirs: I am enclosing a money order for three dollars and would be grateful for a year's subscription to THE BULLETIN of the American Society of Hospital Pharmacists. I am a 1942 graduate of the Ontario College of Pharmacy, University of Toronto, and have been registered as a pharmacist with the Canadian Pharmaceutical Association.

Several friends have loaned me copies of your publication and I have found them very interesting and beneficial. I also subscribe to The Journal of the American Pharmaceutical Association and have been wondering what qualifications I require to become a member of the American Society of Hospital Pharmacists.

Mary E. Asquith

St. Mary's Hospital  
Kitchener, Ontario, Canada

Dear Sirs: With many interests I have read about your Institute on Hospital Pharmacy held in Chicago from May 19-23, 1947. I should be very glad if it would be possible to receive the full reports of the lectures held at this conference. I assure you that you would greatly oblige by rendering your assistance.

J. F. Kok

The Hague, Holland

Dear Sirs: For a number of years I have been a member of the American Pharmaceutical Association, but I feel that I should be a member of the American Society of Hospital Pharmacists too. Enclosed find a check for membership dues. I would also like to receive THE BULLETIN, and if possible, some or all of the back numbers.

Sister M. Wunibalda, S.D.S.

St. Mary's Hospital  
Wausau, Wisconsin

# EDITORIAL

## WHAT THE HOSPITAL PHARMACIST WANTS

All of us at times like to survey hospital pharmacy on a national scale to view its recent accomplishments, present shortcomings, and future potentialities. Of course it is especially important that those who wear the mantle of authority and responsibility in the Society and in the national Association review accomplishments and project planning into the future. But forgetting for a moment the development of hospital pharmacy on a national scale with its many problems of policy, finances, and personnel which involve the resolution of individual positions, and turning to the wishes of the individual member of the Society we find that as a hospital pharmacist he has basic beliefs which involve certain fundamentals.

First he wants the American Society of Hospital Pharmacists to continue as an influential organization because he believes it more fully fills his needs especially because of its influence on a local and regional basis and, equally important, as a uniting force for all hospital pharmacists. He will continue to feel this way until projected plans become realities and until he is convinced in his own mind that the spirit of cooperative sincerity underlies all programs for hospital pharmacy. We have found that hospital pharmacists take a great pride in their Society, probably because they have built and molded its present form themselves, starting with little and growing through the united effort of so many until it has emerged as a small but potent force to cast its influence on probably the most important public health aspect of practicing pharmacy. To so many the Society has brought hope when before there was so little, it has brought pride to replace despair, and it has brought progress and influence, pointing the way toward advancement to those who are willing to make the necessary effort. Memories are not so short nor the idea of projected programs so glittering that the hospital pharmacists are willing to immediately discard the known for the yet to be proved.

The second belief of the hospital pharmacist is that **THE BULLETIN** should be continued in essentially its present form with improvements made as circumstances permit. For through its publication the Society has been able to fill a long sought need, bringing fundamental information, new procedures, discussions of hospital pharmacy policy, professional activities and so

on, which have extended the horizon of professional practice to the most isolated pharmacist as well as to his urban counterpart, letting them know that they too are important to all of us and encouraging them to fulfill more fully their responsibilities in their professional activities.

Then the hospital pharmacist would like to see the Division of Hospital Pharmacy move forward rapidly, not only blazing new trails in the development of hospital pharmacy on a national scale but also making manifest by actions that the Division and those responsible for its activities still have an ear for the pulse of hospital pharmacy and understand the rhythmic beat which repeats the concept that those at the grassroots, the individuals, are the most important persons to be served and only if their needs are filled can loyalty and devotion be earned. An organization is comprised of individuals and where their spirit is, there too lies strength.

Fourth, the hospital pharmacist wants the Institutes on Hospital Pharmacy continued for these programs fill a need not met by conventions, local or regional meetings, or by any other type of assembly. Their perpetuation is fundamental to a more rapid advancement of hospital pharmacy because they give the hospital pharmacist in a short time concepts, practices, and ideas which would take years of experience to develop.

Then, he wants the activities of local and regional chapters fostered and encouraged. From his own chapter the hospital pharmacist obtains constant stimulation throughout the year and the opportunity for a more full participation in the activities of his profession. If plans can be worked out for cooperative meetings with branches of the American Pharmaceutical Association, well and good. If not, no barrier should be placed on the formation of separate chapters for hospital pharmacists. There are still many things which are local problems to be settled only by the organizations and individuals concerned.

Give him these things and the hospital pharmacist will acknowledge that progress in hospital pharmacy continues.

DON E. FRANCKE, *Editor*



## VITAMINS AND TONICS

## Metric

**THIAMINE HYDROCHLORIDE**  
Thiamine Hydrochloride tablets,  
U.S.P. Gm. 0.003  
Gm. 0.005

Vials Steril-Solution Thiamine  
Hydrochloride, M.N.R.  
(60 mg. per cc.) cc. 5.00

**RIBOFLAVIN, U.S.P.**  
Tabs. Riboflavin Gm. 0.001  
Gm. 0.005

**NICOTINAMIDE, U.S.P.** (Niacinamide;  
Nicotinic Acid Amide)  
Tabs. Nicotinamide Gm. 0.05  
Tabs. Nicotinic Acid Gm. 0.05

## VITAMIN C

**ASCORBIC ACID, U.S.P.**  
Ascorbic Acid Tablets Gm. 0.025  
Gm. 0.050  
Gm. 0.10

Amps. Solution of Ascorbic Acid cc. 2.00  
(50 mg. per cc.)

## VITAMIN D (See also under Vitamin A)

**SYNTHETIC OLEOVITAMIN D, U.S.P.**,  
(Vioosterol in Oil)  
(Vioosterol in oil, 5cc. and  
20cc. bottles contain not less  
than 10,000 U.S.P. Units Vit. D  
per Gm.)

## VITAMIN K

**MENADIONE, U.S.P.**, (Vitamin K activ-  
ity)  
Amps. Menadione (in oil), 1cc. Gm. 0.001  
Tabs. Menadione Gm. 0.001

ROCHESTER N.Y. GENERAL HOSPITAL

# THERAPEUTICS

## and

# HOSPITAL

BY DON E. FRANCKE,  
UNIVERSITY HOSPITAL

The preparation of a hospital formulary is one of the most important functions that a hospital pharmacist can perform. Today we are going to discuss the "Therapeutics Committee and the Hospital Formulary" and, of course, both of these subjects are very closely related, one being the function of the other; that is, the formulary is the function of the therapeutics committee. There are several types of formularies some are very simple, compact and concise and others are relatively complex - but one point I would like to emphasize today is that the simple, short type of formulary is extremely valuable and you will make a very fine start if you prepare a short formulary.

The preparation of the longer type of formulary is a difficult and time consuming task. However, if you are able to get your therapeutics committee formed and you are able to prepare a small, compact formulary, even though you are able only to standardize just a few drugs the first time you prepare your formulary it will be of very great value not only to you but to the physicians and also to the hospital. I do not believe that a pharmacist who is working alone in a hospital, or even where there is one other pharmacist, should even attempt to prepare a large several-hundred-page book. I think it would be very foolish because it takes too much time and you just don't have the time to do that and your other work too.

Today I am going to discuss the therapeutics committee, its formation, its composition, its function, and also the role of the pharmacist on this committee. And then I am going to discuss the purposes and advantages and types, and the preparation of a hospital formulary.

### APPOINTMENT OF THE COMMITTEE

Of course, in order to get the therapeutics

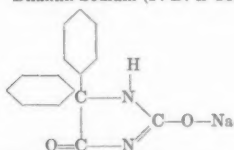
\*Presented at the 1946 Institute on Hospital Pharmacy University Hospital, Ann Arbor, Michigan. Recorded and transcribed by the A.H.A.

54

## FORMULARY AND HANDBOOK

## DIPHENYLHYDANTOIN SODIUM, U.S.P.

Diphenylhydantoinum Sodium  
Dilantin Sodium (P. D. & Co.)



Diphenylhydantoin sodium is employed to depress the hyperexcitability of the motor cortex, upon which it acts with marked specificity. It is used in the treatment of epilepsy and its use is not accompanied with depression of the mnemonic areas of the cerebral cortex.

Dosage—Capsules 0.1 gm. or 1½ grains 2 or 3 times a day. Children under four years of age 30 mg. or ½ grain twice daily.

## ERGOTAMINE TARTRATE, U.S.P.

Ergotaminae Tartras  
Gynergen (Sandoz)

For use in the treatment of migraine. For description and dosage page 68.

## MIXTURE OF COLCHICINE AND POTASSIUM IODIDE

Gout Mixture with Potassium Iodide

	Metric gm. or cc.	Apoth.
Potassium Iodide.....	15	℥ iv
Tincture of Colchicum Seed.....	15	℥ iv
Syrup of Sarsaparilla Co.....	30	℥ i
Water, sufficient to make.....	90	℥ iii

Dosage—4 cc. or 1 dram 3 times a day after meals.

Each dose contains:

Potassium Iodide.....	0.7 gm.	gr. x
Colchicine.....	0.26 mg.	gr. 1/250

JOHNS HOPKINS HOSPITAL

# COMMITTEE

the

## FORMULARY

CHIEF PHARMACIST  
ANN ARBOR, MICHIGAN

committee started, the first thing that has to be done is to have the committee appointed. Usually this is done by the executive committee of the hospital working through the director. It may appoint the entire therapeutics committee, or it may appoint the chairman of the therapeutics committee and let him choose the other members, subject to the approval of the executive committee, but either way works equally well.

### COMPOSITION OF COMMITTEE

Now, the composition of the committee: It is usually composed of a chairman, a secretary, and representatives of various departments. The chairman is traditionally from the department of medicine, because it is this department that uses drugs probably more than any other. The secretary of the therapeutics committee is the pharmacist because he has to be in very close contact with the activities of the committee, and he has to carry out the decisions of the committee.

### NUMBER OF COMMITTEE

The number of representatives on the therapeutics committee will vary a great deal. The usual number ranges from seven to nine, although many hospitals have from three to five on their therapeutics committee. That is something that has to be decided by local conditions. Ideally, I believe the more important services should be represented on the committee, that is, the departments of medicine, surgery, dermatology, obstetrics and gynecology, pediatrics and neurology. If you want to expand the committee further, you can appoint members from various other departments.

### WHO REPRESENTS DEPARTMENT

Oftentimes a question arises as to who should represent the department on the therapeutics

### III. CIRCULATION

#### HEART

##### Pills Digitalis Leaves, N.N.R.

Dispensed in 0.1 Gm. pills, each containing 1 U.S.P. XII unit (approximately equal to 1.3 "cat units").

##### Tablets Digitalis Whole Leaf, N.N.R.

Dispensed in 0.1 Gm. tablets, each containing 1 U.S.P. XII unit (approximately equal to 1.3 "cat units").

##### Digalen Injectable, N.N.R.

Dispensed in 2 cc. ampoules. Standardized by old cat method to contain in 2 cc. 1 "cat unit" (approximately equal to 0.8 U.S.P. XII units).

##### Ampoule Solution Digifoline, N.N.R.

Dispensed in 2 cc. ampoules. Standardized by old cat method to contain in 2 cc. 1 "cat unit" (approximately equal to 0.8 U.S.P. XII units).

##### Quinidine Sulfate, U.S.P.

Dispensed in 0.2 Gm. (gr. ij) tablets.

#### BLOOD VESSELS

##### Amyl Nitrite, U.S.P.

Dispensed in pearls of 0.2 and 0.3 cc. (mij and mv).

Average Dose: 0.2 cc. (mij).

##### Solution Epinephrine Hydrochloride, U.S.P.

1:1,000 Epinephrine Hydrochloride.

Dispensed in 1 cc. ampoules and 30 cc. (℥j) bottles.

##### Erythrol Tetranitrate, N.N.R.

Dispensed in tablets of 30 mg. (gr.ss).

Average Dose: 30 mg. (gr.ss).

##### Tablets of Glyceryl Trinitrate, U.S.P. (Nitroglycerin)

Dispensed in hypodermic and oral tablets, each of 0.3 mg. (gr. 1/200) and 0.6 mg. (gr. 1/100).

Average Dose: 0.6 mg. (gr. 1/100).

Note that metric quantities show either percentage composition or individual doses. In writing prescriptions the total quantity ordered should conform to bottle or ointment jar sizes given on page 2.

24

### 124 UNIVERSITY OF CALIFORNIA

## University of California Formulae

(UC Formulae)

The following formulae represent combinations frequently used in the Out-Patient Clinics and University Hospital. Following each preparation there is given the average dose and directions for use.

#### ABSORPTION BASE CREAM

Absorption Base ..... 50.0  
Distilled Water aa .....  
Aromatics q.s.  
Apply locally.

#### ACETYSALICYLIC ACID COMPOUND TABLETS

Acetylsalicylic Acid ..... 0.22  
Acetophenetidin ..... 0.16  
Caffeine ..... 0.03

1-2 tablets every 3 to 4 hours.

52

UNIVERSITY OF CALIFORNIA

## Drug List

ACACIA, USP—(Gum Arabic) Demulcent; vehicle to suspend insoluble material in water; water solution intravenously for restoring blood volume or for use in nephrosis. Caution: Slowly excreted. Mucilage of Acacia, USP—Syrup of Acacia, NF.

ACETANILID, USP—Phenylacetamide,  $C_6H_5NHCOCH_3$ , M.W. 135; white, odorless powder, poorly soluble in water; readily absorbed from stomach, excreted 4 to 6 hours; analgesic, antipyretic, cardiac depressant. Caution in debilitation and heart disease. Dose: 0.2 gm. in capsules or tablets. Caution on repetition. Compound Powder of Acetanilid, NF, similar to "Bromo-seltzer."

ACETARSONE, NNR—"Stovarsol" 3-acetylamino-4-hydroxyphenylarsonic acid,  $HOCH_2CONHC_6H_4AsO_2(OH)_2$ , M.W. 275; white, odorless, insoluble powder; absorbed from intestines, excreted slowly in urine; contains 27 per cent arsenic; used in treat-

committee, whether it should be the chief of staff or one of his assistants. In order to function strongly and have an influence in carrying out the policies of the committee the nucleus of the therapeutics committee has to be composed of the chiefs of staff. There will be some cases where the chief of staff is not especially interested in this type of work. He may be too busy; and in such instances one of his assistants, a younger man who is very interested in the therapeutics committee will be much more valuable. So, if it comes to a question like that you can always have a younger man on the therapeutics committee and he can confer with his department head concerning questions affecting their particular department.

#### TENURE OF OFFICE

As far as the tenure of office is concerned, I think it far better to make the appointment for one year; that is, you don't appoint a person to the therapeutics committee and just have him remain there. If you do that you'll have a group of people who are not interested. There are always some on a committee who are uninterested and will not attend meetings and will not do any of the work that is required. If you have them on the committee one year, that's long enough. By appointing the committee annually, or having the director appoint the committee annually, you have a chance to replace those individuals who are uncooperative.

#### FUNCTIONS OF COMMITTEE

What are the functions of the therapeutics committee? One function is to serve as an advisory group to the hospital pharmacist, regarding therapeutic agents to be carried by the pharmacy. I would like to make a comment on that; I believe that the pharmacy department headed by the chief pharmacist in any hospital should be an autonomous unit which is responsible only to the director in matters of pharmacy policy. In other words, I do not believe the therapeutics committee should determine pharmacy policy. This committee may make suggestions, and you can take them or leave them after you have talked them over with the director of the hospital. But, as far as the therapeutics committee determining pharmacy policy, I don't think that is their field. I believe that the pharmacist by education and by training is the qualified expert on the preparation and dispensing of therapeutic agents and he is the one who should decide on

matters of strictly pharmacy policy.

I might comment on that a little further. In the Manual of Hospital Standardization published by the American College of Surgeons, under the "Purposes of the Pharmacy and Therapeutics Committee" it says:

"1. It shall determine the policy and operation of the pharmacy," I don't believe that is the function of the therapeutics committee at all. And, it also mentions, "The pharmacy and therapeutics committee should supervise the purchase and issuance of drugs and chemicals." I think that is entirely out of the field of the therapeutics committee. I don't think it should have anything at all to do with that type of work. Those activities are the responsibility of the hospital pharmacist.

The second function of the therapeutics committee is to make recommendations concerning drugs to be stocked on the nursing units. Ward stock medications, of course, will vary a great deal from hospital to hospital and they will vary a great deal with the type of the hospital. I believe in general that it is the practice to have a great number of the less expensive drugs as ward stock. Now, your therapeutics committee may make recommendations to the pharmacist concerning what they believe should be ward stock medications, but it should be the pharmacist in conjunction with the administrator, or the medical director, who should decide what particular drugs are to be ward stock. Physicians are not too well acquainted with the costs of medications and the whole question of ward stocks has to be decided by the pharmacist and the director of the hospital for they affect the overall economics of the hospital.

The third function of the therapeutics committee is to establish a hospital formulary, and I will take up in just a few moments.

Another function of the therapeutics committee is to make periodic reviews of the formulary in order to make additions and deletions. I think you can all see that if your committee did not function along this line it would be a very short time before your formulary would be obsolete.

Another way in which the therapeutics committee can function is to assist in the standardization of prescriptions, and this is an important sphere of activity because the committee can do a great deal to further economy in the hospital and also to promote better service to the patient.

One of the big fields in which medications can be standardized is in dermatology. This is one of the fields of medicine where a great deal of empiricism is still used. I think you will find that if you do have a formulary your dermatologists will stick pretty close to the types of oint-



ments and lotions and other skin preparations that you have listed there. If you don't have a formulary you will have a great number of ointments that will vary in the range of one or two per cent or even less.

Then another type of compounds that lend themselves very well to standardization are synergistic acting drugs like belladonna and phenobarbital. You can pretty well standardize these preparations and if you don't standardize you have a lot of extemporaneous compounding that takes a long time and doesn't allow you sufficient time for other activities.

And then, of course, one of the great fields where the therapeutics committee can help standardize is the vitamins where you have a very large number of preparations to choose from. If you can just take that one class alone and standardize vitamin preparations in the pharmacy and use one particular preparation of each vitamin, and also one B-complex preparation and one multivitamin preparation, your formulary will be of great use to you.

#### SCHEDULE OF COMMITTEE MEETINGS

How often should the therapeutics committee meet? Well, of course, the number of times the therapeutics committee meets will depend entirely on the agenda that is necessary for the committee to cover. After the committee has been functioning for some time, after you have your formulary prepared, then possibly two meetings a year is enough. If you are just beginning the preparation of a formulary and you have a great deal of material to cover, then your formulary committee will have to meet at least every month, and possibly every week or every two weeks. I believe after your committee has been established once, if it meets twice a year that usually is sufficient, but, of course, the secretary or the chairman of the committee can always call meetings if any particular questions arise.

#### ROLE OF PHARMACIST

The role of the pharmacist on the therapeutics committee is to keep the minutes and also to call meetings in conjunction with the chairman. If the chairman has material that he would like to have brought up before the committee, then the pharmacist will call the meeting, and if the pharmacist has material he would like discussed by the committee, he will talk to the chairman and arrange to have a meeting of the therapeutics committee.

Another duty of the pharmacist on the therapeutics committee is to compile data concerning the various medicinal agents and to assist the therapeutics committee in evaluating this material. A great deal of the effort of the pharmacist will be in the economic field. As an example, in selecting a digitalis tablet, the usual procedure would be to get the cost price on a great number of manufacturers digitalis tablets and then to take those figures to the therapeutics committee. Assuming they are all made by reputable manufacturers and they are all U.S.P. products, then the committee would choose the one that was the less expensive. Of course, the same thing is true if you are considering multivitamin preparations, B-complex preparations, or any other therapeutic agents. The pharmacist will gather the potencies of the various manufacturers' products and compare their costs and find the one of good quality that is the less expensive per unit of any particular product.

#### THE HOSPITAL FORMULARY

The next portion of the discussion is on the formulary itself. I have written as a definition "a hospital formulary is a compilation of therapeutically effective drugs and drug combinations which have been collected and passed on by the therapeutics committee and are available from the pharmacy." The purpose of the formulary is to serve principally as a guide for therapy in the hospital, as a guide for prescribing drugs. I think it should be emphasized that the formulary should serve principally as a guide, and you shouldn't say, "here's the formulary, and positively no exceptions will be made in accepting prescriptions for other items". I believe you have to accept prescriptions for other items because there are just countless cases that arise where some special preparation that is not in the formulary will be needed or some common agent in a different form than is in your formulary will be required. And, I believe it is the duty of the pharmacist to supply that material, and I think it is the prerogative of the physician to be able to prescribe it. You have to use judgment and common sense and I believe that in most cases you will find that the medical staff will be very cooperative. Then, in those particular instances where they are not, you can do something about it. As a general policy, it pays to cooperate with the physicians and to furnish what they would like to have, within reason. Of course, in large teaching hospitals, and it is probably true in some of the smaller hospitals which have residents and interns, prescriptions

are written principally by interns and residents. If you have a formulary, that will really be the principal source of their information so they will follow the formulary rather closely.

#### ADVANTAGES OF FORMULARY

One of the advantages of a hospital formulary is that it promotes better and more rapid service to the patient. One means by which it does promote better service is that it allows prebottling and prepackaging of the commonly used preparations so that the medicinals are ready to dispense and the patient does not spend a long time waiting while you compound his prescription.

Then, the advantages to the physician: if the physician looks up a drug in the formulary he will find the English title of the drug, he will find the size and he will find the dosage range. It is a very distinct advantage to him to have a small, concise source of information that he can consult and find the answers to these particular questions in prescribing. Another advantage to the physician and principally true in teaching hospitals, is that the formulary can aid in prescription writing. I think that a great many of the formularies do have model prescriptions and, shall we say, hints on prescription writing. These things, which are seemingly minor in themselves, are of great aid to the intern who has never had much experience along that line.

Another advantage of the hospital formulary is that it furthers economy in medication. It furthers economy by permitting large-scale manufacturing and also by reducing needless duplication in stock. Many institutions will carry from twelve to fifteen brands of digitalis tablets, or vitamin preparations, or multivitamin preparations, or B-complex preparations. If you have a formulary and are able to make it work, you can reduce those to a very few number.

Then, a fourth advantage of the hospital formulary is the advantage to the pharmacist, and I think this is really one of the major advantages so far as we as hospital pharmacists are concerned. If you have a formulary that will allow you to manufacture, the formulary returns manufacturing to the hands of the practicing pharmacist. In the past several years the art of practicing pharmacy, the art of compounding medications has, in general pharmacy practice, left the hands of the pharmacist and you see the condition that pharmacy is in today. I think a great deal of this is due to the fact that we have lost to some extent, really to a great extent, our prerogatives in carrying out manufacturing. Manufacturing removes the pharmacist from the cat-

egory of the pill counter, it makes him use his specialized knowledge that he acquired in school, and it is also an incentive for him to gain more specialized knowledge. Manufacturing increases the pride of the pharmacist. It raises his status in the minds of the physician and the allied professions. In my opinion there are two fields in which the pharmacist can accomplish a great deal to raise his professional status. One is to equip himself to act as a consultant on drugs. Drugs are his special field and he should know more about a broad group of drugs than anyone else. The second is manufacturing. Even a small or moderate amount of manufacturing is splendid public relations, and more particularly, splendid professional relations. The physician will hold the manufacturing pharmacist in much greater esteem than he does the purely dispensing pharmacist.

#### ORGANIZATION OF FORMULARY

The pattern of the formulary will vary with the type of the hospital. Formularies of greater scope are usually required in the open staff hospital. However, their value is not diminished because they do effect standardization to some degree. There are two general types of formularies and I have called them "large" and "small" because I couldn't think of any better terms. The small formularies are arranged in two general manners: in one the drugs are listed alphabetically, that is, all drugs starting from A to Z are just listed straight through the formulary. The second general way in which the formulary is arranged is according to a therapeutic classification with the drugs listed alphabetically within the therapeutic classification. Here are some rather small formularies. This is the formulary of the Massachusetts General Hospital. You see, it is a very small, compact book, but the general way in which the drugs are listed is by a therapeutic classification, and then alphabetically within that classification. Now, the same thing is true of the University Hospital of Cleveland formulary. It also has the therapeutic classification and then the drugs listed alphabetically within that. And this is Tom Reamer's formulary of Duke University Hospital. He adopts the same method, that is, therapeutic classification and drugs listed alphabetically within that.

Now, so far as the type of material that is contained in the smaller formularies which I have mentioned, usually the drug title and the synonym are given, and then the preparation and the dose, either the U.S.P. dose or sometimes a dose range is given. Usually those three items are given



in a small formulary and that is generally the type of information that the physician wants to know. So, if you prepare a formulary classifying the drugs therapeutically and then listing them alphabetically, giving the drug name, its synonym, and the type of preparation; that is whether it is a tablet, a syrup or an ampule, then the dosage range, that type of formulary will be very valuable in any hospital.

There are advantages and disadvantages to the various types of arrangements. If you use the straight alphabetical listing of your drugs, you get away from a lot of duplication. That is about the only advantage of straight alphabetical listing. If you use a therapeutic classification, oftentimes you will have to mention the drug two or three times in various portions of your book. For example, atropine sulfate would be listed under parasympathetic depressants and also under peristaltic depressants. The same type of thing is true of benzedrine which would be listed under two general classifications.

Larger formularies are used principally in teaching institutions. In this type of institution where you have a very large number of interns, the formulary will be more valuable if, in addition to the drugs themselves, there is also a short statement on the actions and uses, the route of administration, the side effects and toxicity and, if it is a potent drug, the antidote for that particular drug.

Here are examples of the larger formularies. One is the formulary of the Johns Hopkins Hospital which is an excellent one. It contains the official title of the drug and then a statement on the actions and uses and then a statement on the dosage of the drug. That general arrangement is followed all the way through the book. The other is the formulary of the University of Michigan Hospital.

#### RULES FOR INCLUSION OF DRUGS IN FORMULARY

What sort of rules is the pharmacy committee going to follow? What standards are they going to have for accepting therapeutic agents or rejecting them? I think that is a policy that has to be developed by every therapeutics committee. The New York Hospital has published their rules for admitting drugs to the formulary, and I shall give you a reference on these rules because I think you might want to consult them at length. One reference is the Journal of the American Pharmaceutical Association, December 1933. And another source is the Modern Hospital, Volume 52, No. 4, April, 1939.

Now, I'll rapidly go through some of these rules that are used to govern policy in the New York Hospital because I do think they can serve as a guide for any therapeutics committee. The committee can use these as a guide and adapt their own rules to fit local conditions.

"No. 1. Simple official substances and any in "Useful Drugs" will be admitted when requested, unless they have become superfluous.

No. 2. No article will be admitted, except for controlled research, before its therapeutic value has been established.

No. 3. No article of secret composition will be admitted.

No. 4. No article that is sold under a proprietary name will be admitted under such name if a substance of identical composition can be obtained under a non-proprietary name.

No. 5. No mixture of two or more substances will be admitted unless evidence is submitted that the mixture presents therapeutic advantages over the simple substances.

No. 6. No proprietary article will be accepted before it is accepted by the Council on Pharmacy and Chemistry of the American Medical Association for inclusion in "New and Nonofficial Remedies".

No. 7. It is the policy of the committee to discourage the intravenous and intramuscular injection of substances which should be administered orally.

No. 8. The pharmacist is instructed to supply in emergencies preparations not yet accepted by the formulary committee.

No. 9. The pharmacist will stock and supply drugs requested on the private or semi-private services even though they have not been accepted by the formulary committee.

No. 10. Heads of clinical departments are to be notified whenever any preparation is considered for elimination from the formulary in order that they may submit evidence for its retention.

No. 11. The chief pharmacist is instructed to issue drugs under rules governing the formulary committee subject to the approval of the medical board.

No. 12. All actions of the formulary committee are subject to the approval of the medical board."

That gives you a very broad picture of the type of rules one leading teaching institution has adopted for the admission of articles to its formulary, and you can adapt those rules and use them as a nucleus for your own local conditions.

In our hospital all official preparations, that is, all U.S.P. preparations and N.F. preparations, are furnished under the official title, and



if the physician orders an official drug under a trade name we furnish him a U.S.P. or N.F. product. This policy is understood and accepted by the physicians on the hospital staff.

### PREPARATION OF FORMULARY

Now, as far as the preparation of the formulary is concerned: The initial step is to have the therapeutics committee appointed. The next thing is to decide who is going to write the formulary. I believe that in most, if not all instances, the pharmacist should write the formulary because he has a very much closer contact with drugs than does the average physician, and he has, or should have, a very broad knowledge of the actions and uses of drugs. The pharmacist will begin writing the formulary and as the material progresses the manuscript will be read by the members of the therapeutics committee and will be criticized and additions or corrections will be made. Also, your various department heads will be consulted as to the types of drugs or preparations they would like to have included in the formulary.

You also have to decide the type of formulary you are going to compile, that is, are you going to compile a smaller type formulary where you will list the titles and synonyms and dosage and preparations of the drug, or are you going to compile the larger type where you will go into things a little more in detail.

There are a number of other questions that will arise when you begin compiling your formulary. One of these is whether you should include hospital routines. You will find that some formularies include hospital routines. The Johns Hopkins formulary has some hospital routines, the University of California Formulary has a great number of hospital routines. I do not think it is advisable to include them in the formulary for the simple reason that practically all of your services have manuals of procedure which they use in their department. Routines take up a lot of room in the formulary and you can't have the procedures as complete. However, items that will be very useful to include in your formulary, in addition to drugs, are conversion tables and narcotic regulations, and even just a page or two on prescription writing will be a great help to the interns.

If the pharmacist is now ready to write, how does he begin to make his formulary? Well, one of the first steps that he has to take is to make an outline of the therapeutic classification of drugs and then arrange the drugs within that therapeutic classification alphabetically. For

example, he may start out with the central nervous system drugs: the central nervous system depressants including the sedatives and hypnotics and analgesics and antipyretics, and make a very broad therapeutic classification of all the drugs he may wish to include within these categories. The next step will be to prepare monographs of the individual drugs selected.

There are several things which must be considered when deciding on the format of your formulary. You have to decide about the size of your book and, of course, the smaller you have the book, within reason, the easier it will be to use. I think all of these books are ones that fit in the intern's pocket, and that is what he wants, something he can carry around with him all the time and have as a handy reference. So in deciding the size, be sure that you get one that will fit in the intern's pocket. The maximum size is about seven by five inches.

Then, another very practical consideration in making your formulary is to be sure that your formulary lies flat when open. Now this particular book has to be held open when being used and it is quite difficult for the intern to use. It would be much easier to use if it did lie flat on the table. If, instead of having individual cut pages as these are, the formulary had just been printed on double pages and then stapled through the back, the formulary would lie flat. That is just one of those little items that makes a formulary much more useful.

The question arises as to whether to use the metric system or the apothecary system. Probably most formularies use both systems. In our formulary we use only the metric system, in fact, in our hospital we use only the metric system. And that is just one of those things you have to decide, based on local conditions. Many of the older men in practice are used to the apothecary system and for that reason it is often a good idea to include both systems.

Another question that arises is whether you should include the formulas for drug combinations. For instance, we have one preparation called "elixir of bellarbital" which consists of elixir of phenobarbital and tincture of belladonna. The formulas for all hospital preparations should be listed in the formulary if they are going to be of any value to the intern after he leaves, because if he orders them in some other hospital by your localized name nobody will know the ingredients or the formula.

I have passed out some of the Michigan hospital formularies to most of the tables and you can see the way in which the formulary is arranged from the table of contents. Then turning to the individual drugs, for example under Ben-

adryl are given the specific action and the uses of the drug, its side effects, and the side effects that are more prevalent; the dosage; and the forms available for oral use and for injection. The same general plan was followed under the antibiotics: the description of penicillin, its dosage, routes of administration, the dosage of penicillin by injection, for oral use, and for inhalation; and the strengths and preparations of penicillin that are used for topical application are included.

### DISCUSSION

**MR. LAUVE:** That was a very interesting lecture on "The Therapeutics Committee and the Hospital Formulary." I am just wondering if anyone is interested in asking Mr. Francke some questions, possibly to verify some of his statements.

**MR. ZUGICH:** What are the advantages of listing the chemical formula, say in the general hospital outside of a teaching hospital?

**MR. FRANCKE:** Listing chemical formulas in a formulary has two advantages: First, it gives the physician an idea of the close chemical relationship between compounds. For example, pavatrine and trasentine are closely allied chemically as well as therapeutically, differing only by the addition of a double bond. Hexestrol and diethylstilbestrol are also similar, differing only by one carbon atom and a double bond. Also, I believe it is valuable for the physician to note the chemical relationship among the various sulfa drugs. The second advantage of listing chemical formulas is that they tend to break up the page and to make it more attractive. I think they are really worthwhile for both of these reasons.

**MR. SOUTH -** I would like to ask Mr. Francke what his opinions are on looseleaf hospital formularies. I have one with me with a ring binder. I see one advantage. It lies flat. You were speaking about that.

**MR. FRANCKE -** Well, I think a looseleaf formulary of the ring type is the best type of looseleaf formulary. Most of the looseleaf formularies that I have seen are more of this type, where in order to insert another page you have to unscrew both binding-posts and then put them back together, and I would doubt that more than one physician in a hundred ever bothers to put any additions in a looseleaf booklet like this. The ring type would be entirely different because it is so easy to open and you can just insert your page. There certainly are advantages to a formulary of this type. It's a good size and when you have ring bindings, of course, it's very easy to use and that's really what makes it good.

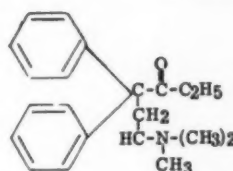
### UNIVERSITY OF MICHIGAN HOSPITAL

#### ANALGESICS AND ANTIPYRETICS

127

#### METHADON HYDROCHLORIDE

Amidone, Dolophine, Adanon



Methadon is an analgesic drug with pharmacological actions closely resembling those of morphine. Its habit-forming liability has not yet been fully determined. Its analgesic potency in therapeutic doses probably lies between that of merperidine

and morphine. Like morphine, it depresses the respiration and produces an increase in the tone and amplitude of intestinal contractions. It produces less sedation and narcosis than does morphine. Methadon is an antitussive.

Side effects include, in the order of their frequency, nausea, vomiting, lightheadedness, drowsiness, dryness of the mouth, perspiration, and mental depression. Miosis occurs after repeated administration of the drug but tends to disappear with continued use. The side effects are usually mild and may be observed after oral or parenteral use of the drug.

Methadon is used to control postoperative, renal colic, osseous and other types of pain. It may be used to suppress coughing. The drug is not a good preanesthetic agent since it does not produce sufficient euphoria or sedation. It does not compare favorably with other analgesics in the relief of labor pain.

#### Dosage:

Methadon may be given orally, or by intramuscular or intravenous injection. The dose range is from 2.5 to 10 mg given orally or parenterally every 3 to 4 hours. The antitussive dose is 1.5 to 2 mg.

#### Preparations:

Injection Methadon 10 mg per cc; 1 cc; 20 cc.\*

Syrup Methadon 2 mg per 4 cc.\*

Tablets Methadon 2.5 mg; 5 mg; 7.5 mg.\*

\*Narcotic Prescription

**MR. SOUTH -** Did the formulary committee help you and how much help did you get out of them?

**MR. FRANCKE -** Well, of course, a committee is a great thing. Actually, at the time our formulary was prepared we happened to have three members on our formulary committee, two of them were in the armed forces and the other member came to me and asked me to prepare the formulary, which I did. In preparing the formulary probably the major consultation that was done was in the field of dermatology preparations where there are a vast number of items that are ordered in combination. Those drugs and drug combinations were listed on cards and then reviewed with the chairman of the Department of Dermatology. As you will notice, this is one of the larger sections of the formulary, one which I think is too large, but maybe in the next edition we shall be able to correct that.

# AMPULS



By LEONARD YODER\*

EUNICE ANDERSON ROYER\*\*

H. GEORGE DEKAY\*\*\*

Ampul manufacture will be considered only within the limitations set by the N.F. VIII definition of ampuls as ". . .hermetically sealed containers commonly made of glass and, when filled, contain sterile preparations, usually solutions or suspensions of drugs, intended for parenteral use."

## HISTORY

Ampuls were first used as containers for hypodermic medication in France. The Bulletin Generale de Therapeutique of April 15, 1886 published an article by Limousin<sup>1</sup>. In this article Limousin described "ampoules hypodermatique" for the preservation of hypodermic solutions in a sterile condition. The ampul of Limousin was a spherical bulb holding a little over 1 cc., with a finely-drawn-out neck about 1 1/4 inches long. Little attention was paid to this new form for dispensing medications in this country until about 1909. From 1913 to 1919 there was an increased interest in ampuls in this country with many articles published on small scale ampul manufacture, apparatus and requirements. As their popularity increased, standards for uniformity and purity were set up and manufacturing houses listed an increasing variety of ampuls in their catalogues, especially for biologicals and related medications. Today the use of ampuls as a form of dispensing medications is well established and



is of increasing importance to the hospital pharmacist.

## EQUIPMENT

The first consideration in ampul manufacture is the space and equipment to be used. If possible a special room should be equipped for this purpose. This room should be dustproof, have special air conditioning with easily changed air filters. The walls should have a smooth finish, and all furnishings should be easily cleaned. The following basic equipment is suggested: blow torch (with gas, air and oxygen valves), gas, air and oxygen supplies, still (preferably of all glass parts), a very accurate balance, sintered glass filters, suction bottles and high pressure tubing, burette stand, burettes (glass stopcock), autoclave (10"), suitable containers for holding ampuls during sterilization, 1000 cc. Erlenmeyer flasks, graduates, stirring rods, rubber tubing, T-tube, pinch clamps, volumetric flasks, beakers, spatulas, hypodermic needles (2" x 10), weighing glasses, and vacuum dessicator. The exact sizes of the various flasks, graduates, and so on, will depend upon the needs of the individual hospital. The personnel working in an ampul room should wear masks, caps, and special garments which cover their regular clothing completely.

## AMPUL GLASS

The glass of which the ampuls are made is important. Only glass of the hardest variety, which can stand up under intense heat and will not chip, should be used. Such glass must be insoluble in water and not impart alkalinity. Soft or poorer grades of glass are soluble in water,

\*Graduate Student At Purdue University

\*\*Four years experience in Civilian and Military Hospitals

\*\*\*Professor of Pharmacy, Purdue University



they deposit needle-like crystals, which if injected might cause death. Alkalinity in glass leads to such problems as precipitation of alkaloidal medicinals, inactivation of some substances and irritation at the site of injection.

Mayo<sup>2</sup> recognized the importance of neutral glass for ampuls as early as 1909. He found the first glass which met neutral requirements was the Jena Normal, 16, III, a product manufactured in Dormstadt, Germany. Mayo suggested testing ampul glass by filling the ampuls with a phenolphthalein solution, sealing, and then boiling them for one half hour. Alkalinity was indicated if the solution became pink. After considering a number of different methods of testing for alkalinity, it was concluded that a variation of Mayo's test was the easiest and most reliable. The sealed ampuls were autoclaved at 15 pounds pressure for 15 minutes instead of boiled.

In 1919 Eli Lilly & Co.<sup>4</sup> submitted an article suggesting a procedure for testing alkalinity in ampul glass which corresponds very closely to the present day assay of the N.F. VIII. To conduct this assay a representative sample of six ampuls are cleaned, rinsed thoroughly and dried. The dry ampuls are reduced to a fine powder in a steel mortar and that portion which passes through a number 40 sieve but not through a number 50 sieve is used for the test. A magnet is used to free the powdered glass from steel particles. Ten grams of the dry powdered glass and 40 cc. of ampul water are placed in a resistant glass flask (125 cc.) Forty cc. of ampul water is placed in a similar flask. The flasks are capped and autoclaved at 15 pounds pressure (121.5° C.) for 30 minutes, cooled at once and titrated with N/50 sulfuric acid, using phenol-red as an indicator. The amount of sulfuric acid used for the blank is deducted from that consumed in the glass mixture and difference should not be more than 0.6 cc for the ampul glass to be acceptable.

In 1939 Snyder<sup>9</sup> suggested the Kimble titration method for distinguishing between resistant and soft glass containers. To distinguish between treated and untreated soft glasses, he used either the electroconductivity or the residue method. The later method is not very reliable for distinguishing between resistant and treated soft glass since the values obtained are too close. Due to different size containers, allowance must be made for the difference in the ratio of the area of glass exposed to the volume of water. Snyder also states that the water-soluble constituents, mostly sodium silicate, apparently have no pharmacological importance. However, he is not willing to state this as a fact, as he had not made a sufficient number of tests.

A number of ampuls of various sizes and composition were tested in the laboratory by a method similar to the ones suggested by Mayo<sup>2</sup> and Ewe<sup>5</sup>. Some of these ampuls were commercially prepared and others were made in the laboratory from pyrex glass tubing. The ampuls were boiled in distilled water containing 0.1% HCl, rinsed twice with redistilled water, filled with phenolphthalein solution, sealed and autoclaved. They were autoclaved at 20 pounds pressure (260° C.) for 30 minutes. Upon cooling the color of the solution was noted and all commercial ampuls and those made from pyrex tubing were found to be acceptable as the solution was colorless. This test is very easy to carry out and is believed to be a reliable method for testing ampuls for the alkalinity of glass.

#### PRELIMINARY PREPARATION OF AMPULS

Commercial ampuls should be carefully cleaned before they are used, as they may easily become dirty between manufacture and the time they are used. Materials commonly found in empty ampuls include dust, fibers from packers and glass particles. The literature describes a number of procedures to be used for cleaning the ampuls before they are filled. The earliest method<sup>3</sup> suggested cleaning the ampuls with a 5% phenol solution, then rinsing with distilled water and drying in an oven, while other methods suggested blowing the ampuls out with compressed air<sup>18, 14</sup>. Several chemicals have been suggested, including 1% sodium metasilicate<sup>7</sup> potassium dichromate-sulfuric acid solution<sup>8, 10</sup>, trisodium phosphate solution<sup>14</sup>, and dilute acid solution with boiling. These chemical washings dissolved the material clinging to the glass, and the ampuls were then rinsed several times with distilled water, finally with redistilled water and dried in a hot air oven.

In the laboratory several methods were tried and it was found that the use of a dilute acid solution was the most practical and safe method. The complete removal of some other chemicals was difficult and unreliable. The ampuls were boiled in a 0.1% HCl solution for five minutes, being certain that all ampuls were completely filled before timing was started. It is important that the ampuls be filled completely as the object of the acid solution is to remove any excess alkalinity from that part of the glass to be exposed to the ampul solution. After boiling, the ampuls were rinsed twice with distilled water and then with redistilled water. The rinsed ampuls should be inverted in a suitable container and dried in an oven, if they are not to be used within a short time.

A simple rinsing apparatus may be constructed from the following: A hypo needle is connected

to a T-tube. Rubber supply tubes, with a pinch clamp on each, are attached to the other arms of the T-tube and are in turn connected to a distilled water supply and an air supply. By using the pinch clamps alternately, the ampul placed over the hypo needle can be filled and blown out very quickly.

There is some controversy about the necessity of autoclaving the clean ampuls before they are used. Most authors feel that this preliminary sterilization is important, and certainly should be carried out if the ampuls are not to be used within a few hours. Pyrogens are formed very readily in the distilled water left adhering to the inner surface of the ampuls after rinsing.

#### PREPARATION OF SOLUTIONS

In preparing even the simplest solution to be used in ampuls every possible precaution should be taken to prevent contamination and assure accuracy. If possible a special dust-free room should be equipped to prevent contamination from air-borne bacteria and dust. The balance used must be very accurate as the quantitative limits of the active ingredients are narrow and should be strictly adhered to. Ampuls are intended for parenteral use so that the active ingredients can be rapidly absorbed and made available to the system. The injection quantity must be accurate to obtain the desired action.

All equipment should be very clean. After washing it should be rinsed with distilled water. If the equipment is to be used immediately, it should be rinsed with freshly redistilled, pyrogen-free water. It is advisable at all times to keep a complete set of clean, sterile equipment for the preparation of solutions, and filling of ampuls, so that they can be readily available in case of an emergency call.

Water for ampul solutions should be freshly redistilled. The N.F. VIII directs that ampul water should be redistilled from distilled water to which has been added 10 cc of potassium permanganate T. S. and 10 cc of sodium hydroxide T. S. per liter. Solutions should be sterilized within three or four hours after the water is redistilled to prevent the formation of pyrogenic substances. It may be a good policy to keep on hand a supply of sterile ampul water that has been sterilized shortly after distillation. This water can be kept in hermetically sealed flasks or in flasks with paper closures. In the latter case it is not advisable to use the water if more than a week has elapsed after it was sterilized.

Most pharmacies use U.S.P. grade chemicals in compounding prescriptions and other manufacturing work. But in the manufacture of ampul solutions it has been recommended that chemicals with a higher standard of purity be used. Chem-

ically Pure or Reagent Grade chemicals are best.

Although special care has been used in making the solutions, they should always be filtered. A sintered glass filter, Seitz filter or sharkskin filter paper were found to leave the fewest particles in the filtrate. Any filter paper used should be washed with redistilled water or other suitable solvent before filtration to remove the linters that usually adhere to dry filter paper. With the sintered glass and Seitz filter a vacuum system is necessary and one attached to the water faucet is adequate.

#### AMPUL FILLING

Since the first ampul was manufactured, many attempts have been made to make an accurate, simple ampul filling apparatus. There are innumerable kinds described and illustrated in the literature. But they have the common disadvantages of being extra pieces of apparatus and usually are complicated and difficult to clean. Although most of the machines and apparatus suggested for filling are intended to make the work easier and avoid contamination of the solution, they are usually complex in construction and so the reverse is true. Cleaning and setting up of such equipment involves considerable time. The more equipment and parts involved the greater are the chances for contamination.

In the laboratory it was found that a burette fitted with a large bore hypodermic needle was very accurate, easy to manipulate, and clean. These items are usually available in any pharmacy. The burette can be refilled in a closed system composed of tubing with clamp and a supply bottle. A two holed rubber stopper is used in the top of the burette, one for the supply inlet and the other with an air filter to allow the air to enter the burette as the ampuls are filled. With a little practice it is easy to introduce the hypodermic needle into the neck of the ampul, and also to remove it without touching the inside of the neck and leaving some of the solution on the inner walls. If a few ampuls are to be filled, a large sized hypodermic syringe may be used, but the accuracy is not as good as with the burette.

#### SEALING

Sealing ampuls is dependent upon two main factors, the flame used and the skill of the operator. A good seal is obtained consistently with a little practice. The flame should be an oxygen-gas-air combination. A small pin-point flame about two or three inches long is very good. Because most ampuls are of pyrex or other similar hard glass, the ordinary gas-air flame is not hot enough. There are several torches on the market that will produce this type of flame.



The tip of the ampul may be rotated evenly in the flame until a seal is made, but it left a fraction of a second too long a bubble may be formed in the molten glass at the tip of the ampul. Such a bubble is a weak spot in the ampul and may be broken very easily. Another method of sealing is by using a glass rod. The ampul neck is rotated in the flame about one-half inch from the tip and as the glass becomes molten the excess is pulled off with a glass rod. This method is faster, is more certain of sealing, but does not give as smooth a seal. With either method proficiency is the result of practice.

#### LEAK TESTING

After the ampuls are sealed they should be tested for leakers. A simple test is to place the ampuls in a solution of methylene blue, heat the solution and allow it to cool. When the ampuls are heated, the air is forced out of leakers, then when they cool the blue solution is drawn into the ampul and leakers can be easily detected. However, the ampuls in the methylene blue solution can be placed in a vacuum dessicator. When a vacuum is applied the contents will be drawn out of any leakers and normal pressure will force the colored solution into them. Also any leakers may be detected during autoclaving, if the chamber is vacuumed before it is filled with steam. If a leaker is present, all or part of the solution will be drawn out of the ampul at this time, and the partially filled or empty ampuls can be easily detected. This method is particularly good with larger ampuls and the ampuls should be placed in the holder with the tip end down. All ampuls should be tested for leakers as even the most proficient operator may not always make perfect seals. Also other parts of the ampuls may have minute openings, which were left during the manufacture of the empty ampuls.

#### CLARITY

Inspection and interpretation of the clarity of ampuls are indefinite<sup>16</sup>. The N.F. VIII states that the finished ampuls must be substantially free of all turbidity or undissolved material which can be readily detected. Ampuls are viewed against black and white backgrounds by means of reflected light. The difficulty lies in trying to interpret what is meant by "substantially free" as each person may give the term a different meaning. Another variation may be the result of the visual ability of each individual. In the testing for clarity it is best not to look at each ampul too long. Frequent rest periods should be taken to prevent eyestrain with the resulting inability to judge the clarity of the solution correctly.

#### STERILIZATION

The sterilization of ampuls during manufacture is a very important step. All of the precautionary measures taken prior to sterilization are of no value if the sealed ampuls are not properly sterilized.

The most common method used in sterilization is autoclaving. The ampuls are usually subjected to steam sterilization at 260° F and 20 pounds pressure for 15 minutes. Most ampuls can be autoclaved without any deterioration of the active ingredients. This is the desired method wherever possible, as it is effective and simple. If an ampul room is being equipped, a small 10 inch autoclave should be part of the original equipment. This size is adequate for the sterilization of the number of ampuls which usually would be manufactured at one time in a hospital.

If the material in the ampul is of such a nature that it will deteriorate at high temperatures, fractional sterilization is used. The ampuls are suspended over water in a closed vessel and are heated until the desired temperature is reached in the chamber. This temperature is maintained for 30 minutes. The process is repeated on the next two successive days. The ampuls are kept at room temperature between heating periods, so that any spores present may develop into vegetative forms and be killed at the next day's heating.

Material which cannot be subjected to heat may be sterilized by a Berkefeld type filter. Great care must be taken to insure sterility of all pieces of equipment and of the ampuls. Aseptic technique must be maintained throughout the process. Filling should be under a glass hood. Ampuls so handled must also meet the official N.F. test for sterility.

Another interesting method of sterilizing ampuls was found in the literature. Gunther<sup>6</sup> suggested the use of ultraviolet light rays. All solutions were found to be sterile after 30 minutes exposure to a 200 volt quartz lamp at a distance of 50 cm. The value of this method has not been fully established, in that insufficient work has been done with it.

#### STERILITY

After each lot of ampuls is manufactured, bacterial culturing is carried out on a representative sample to make certain that the lot is free from bacterial contamination. It is recognized that even though a lot of ampuls has been manufactured under the most sanitary conditions and are thought to be properly sterilized, the possibility of bacterial contamination is still present. For the purpose of testing sterility, injectable ampuls have been classified into the



following four groups:<sup>11</sup> 1. biologic, 2. bactericidal chemicals, 3. chemicals in which bacteria may grow, 4. chemicals - not bactericidal but not conducive to the growth of bacteria. Bacterial culture tests should always be run on groups 1, 3 and 4. Bacterial culturing must be carried out under aseptic conditions in order to obtain true results as to the sterility of the solutions in the ampuls tested. Nutrient agar plates and lactose broth tubes are inoculated with fluids from the ampuls. Oily suspensions require special modified media, and the operator must select the media required. Plates or tubes are incubated at 37.5° C for 48 hours and then examined for growth. Clear plates or broth tubes are an indication of sterility. Failure to obtain these conditions requires further testing to confirm the results.

The N.F. VIII give instructions for the running of sterility tests, and lists the methods for the preparation of culture media of different composition.

#### PYROGENS

Pyrogenic substances have always given trouble in parenteral medications. The chemical composition of pyrogenic substances varies with the types of microorganisms that produce them.<sup>13, & 15</sup> They are not destroyed by ordinary sterilization procedures; so, it is necessary to prevent their formation by using freshly redistilled water. In redistilling water the addition of potassium permanganate and sodium hydroxide insures the removal of all oxidizable or reducible material. After the water has been redistilled it should be used within 3 or 4 hours in making an ampul solution, or unused redistilled water should be sterilized within this time for use later. Todd and his co-workers<sup>17</sup> claimed that pyrogens could be removed from saline and other solutions for intravenous use by adding 0.02% purified carbon and filtering through a Seitz filter prior to sterilization. Although this method is good, it is time consuming and unnecessary if proper precautions are taken to insure the use of freshly redistilled water. To make certain that the solutions are pyrogen-free it has been found necessary to run pharmacological tests, using rabbits as the test animal. According to the U.S.P. XIII the rabbits should weigh over 1550 Gm. A minimum of three rabbits should be used for each test. Rabbits used for pyrogen tests are not contaminated and may be used for further tests in the Bacterial Laboratory, thereby cutting down on the expense of the work. The rabbits should be housed in a constant temperature room during the test and care should be taken to avoid excitement. Rectal temperature for each rabbit should be established.

Food should be withheld from the animals beginning one hour before the first temperature reading, following injection, and during the time of the test. The solution to be tested should be warmed to 37° C before injection, using 10 cc per kilogram of rabbit. Syringes and needles should be rendered pyrogen free before using. Three temperature recordings should be made starting one hour after the injection. The test is considered positive if two or three animals show an individual rise in temperature of 0.6° C or more above the normal established for each of the animals.

Chapman<sup>12</sup> believes that this method of pyrogen testing is unreliable as the temperature of the rabbits may be affected by influences other than the injected solutions. Rabbits are easily excited and this alone may cause a confusing rise in temperature. He believes a leucocyte count is a more reliable method. The outside influences could not affect the count but the presence of pyrogens produced a definite leucopenia in the test animals. Chapman's method sounds interesting but more complicated and is not the official method as given in the U.S.P.

The official U.S.P. method as outlined above was carried out in the laboratory with satisfactory results. One rabbit did become excited during the test with a marked rise in temperature, but the others showed very slight if any rise in temperature.

#### ASSAY

Assays should be carried out according to the procedures listed in the individual monographs in the U.S.P. and N.F.

#### CONCLUSIONS

Small scale ampul manufacture may be undertaken by almost any hospital pharmacist. Such work usually is a special convenience for the doctors, and requires considerable time on the part of the pharmacist, but it enhances his professional prestige. The general procedures may be varied if rubber capped vials or other containers are to be used.

#### BIBLIOGRAPHY

1. Mayo, C. A.: Ampuls and Their Use in The Dispensing of Hypodermic Solutions; Merck's Report, 18, 33, 1909.
2. Mayo, C. A.: The Ampul From the Retail Druggist Standpoint; Am. Druggist and Pharm. Record, 54-55, 98, 1909.
3. Anon; Ampules; Yearbook Am. Pharm. Assoc., 2, 30, 1913.
4. Anon; The Manufacture of Ampoules; Am. Druggist and Pharm. Record, 67, 518, 1919.

5. Ewe, G. E.; The Selection of Glass for the Manufacture of Ampuls.; *Amer. J. of Pharm.*, 92, 581, 1920.
6. Gunther, G.; New Method of Sterilization of Ampules.; *Pharm. Monatsh.*, 5, 177, 1924; *Abst. in Yearbook Am. Pharm. Assoc.*, 13, 34, 1924.
7. Anon; Ampuls, Thank You.; *Drug and Cosmetic Industry*; 37, 264, 1935.
8. Lesser, M. A.; Ampoules; *Drug and Cosmetic Industry*, 40, 494, 1937.
9. Snyder, R. K.; The Chemistry and Pharmacology of the Soluble Constituents of Ampul Glass.; *J. Am. Pharm. Assoc.*, 28, 7, 1939.
10. Foss, N. E.; Chromic Acid Wash Held Best for Ampul Clarity.; *Squibb Abstract Bull.* 14, 732, 1941.
11. Blumberg, B. L.; Sterility Tests on Chemical Preparations for Parenteral Use.; *J. Am. Pharm. Assoc., Sci. Ed.*, 31, 245, 1942.
12. Chapman, C.; The Use of Rabbits for the Detection of Pyrogenic Substances in Solution for Intravenous Administration.; *Quart. J. of Pharm.*, 15, 361, 1942.
13. Co Tui and Schrift, M. H.; Production of Pyrogens by Some Bacteria.; *J. Lab. Clin. Med.*; 27, 569, 1942.
14. Light, Amos E.; Apparatus for Rinsing Small Mouth Bottles.; *Chemist-Analyst*, 32, 21, 1943.
15. Robinson, E. S. and Flusser, B. A.; Studies on Pyrogens I The Isolation of Pyrogens from Various Microorganisms.; *J. Biol. Chem.*, 153, 529, 1944.
16. Godding, E. W.; Foreign Matter in Solutions for Injections.; *Pharm. J.*, 154, 124, 1945.
17. Todd, J. P., Laurie, J. T. and Milne, G. R.; The Preparation of Non-pyrogenic Saline Infusion Fluids.; *Pharm. J.*, 156, 156, 1946.
18. Chilson, F.; Shock Washing.; *Drug and Cosmetic Industry*, 55, 1944



## new members

### ARIZONA

Bernard A. Bialk, Assoc.  
Route 2, Box 551  
Tucson

### INDIANA

Kenneth R. Gillmore  
1603 Central No. 214  
Indianapolis

### KANSAS

Marley G. Rowe, Assoc.  
135 N. Main  
Wichita

### MARYLAND

Sr. Margaret M. Mooney  
Caton & Wilkens Ave.  
Baltimore

Kenneth G. Spangler  
1728 N. Montford Ave.  
Baltimore

### MASSACHUSETTS

Vincenzo A. Cervizzi  
282 Sumner St.  
E. Boston

Edwin W. Spear  
182 Fairmont Ave.  
Hyde Park

### MICHIGAN

William E. Romps  
9124 Northlawn  
Detroit

### MISSOURI

Merle E. Duryee  
3543 Washington Ave.  
St. Louis

### NEBRASKA

Louise Becker, Assoc.  
141 No. 41st St.  
Omaha

Charlotte E. Cox, Assoc.  
Sutherland

### NEW YORK

Bess Cabibbo  
99 Madison St.  
New York

William E. Chandler  
P. O. Box 43  
Batavia

Dean B. Joslyn  
370 West Clinton St.  
Elmira

Sr. M. Eugenia Wood  
St. Peter's Hospital  
Albany

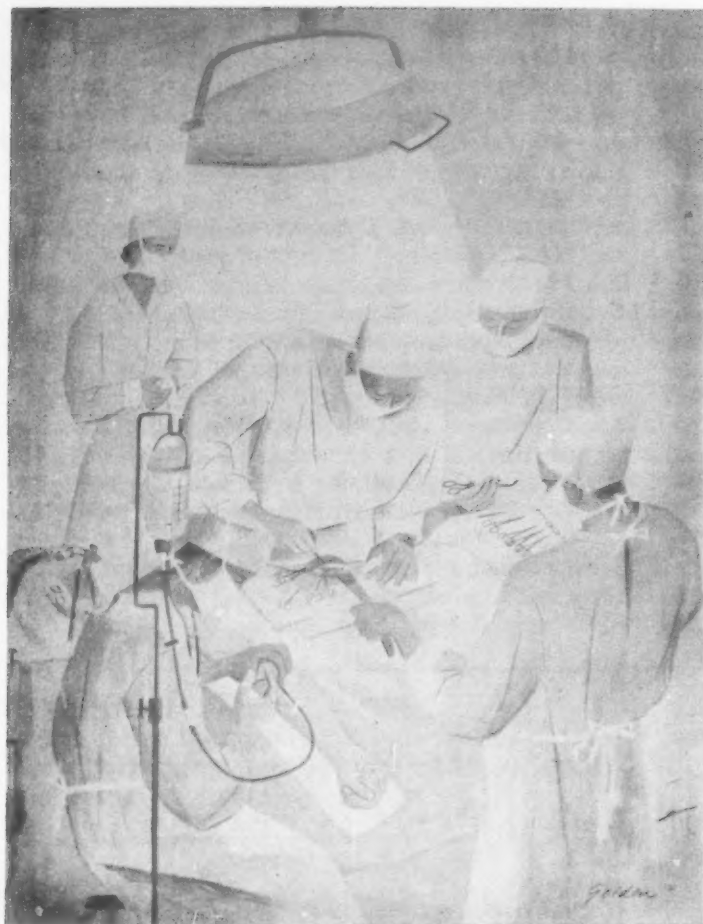
### PENNSYLVANIA

Robert Garrison  
3909 Walnut St.  
Philadelphia

O. J. Inashima  
Jefferson Medical  
College Hospital  
Philadelphia

Sybil D. Lipson  
1057 South 52nd St.  
Philadelphia

Jean Whitmore  
Jefferson Medical  
College Hospital  
Philadelphia



# *Evaluation* of GERMICIDES

AN IMPORTANT FUNCTION OF THE PROGRESSIVE HOSPITAL PHARMACIST IS TO ASSIST IN THE EVALUATION OF GERMICIDES. THIS CURRENT ARTICLE IS PRESENTED HERE TO HELP HIM IN THIS TASK.

## **Council on Pharmacy and Chemistry**

### REPORT TO THE COUNCIL

#### ORGANOMERCURIAL COMPOUNDS

The Council on Pharmacy and Chemistry presents the following report by Drs. Morton and North and Mr. Engley as a further challenge to the scope of usefulness of mercurial antiseptics. The potency of mercury, as either an inorganic or an organic compound, to inhibit growth in bacterial cultures is so striking that it created the presumption of high disinfectant potency. This presumption was severely shaken when it was proved that the inhibited bacteria are not killed by the mercurials but resume lusty growth when the adherent mercury is sufficiently diluted or when it is removed chemically by sulfur compounds. Nevertheless, the use of mercurial antiseptics has continued, especially in the form of organic compounds of low systemic or local toxicity. This could be defended in a degree on the basis that bacteriostasis would at least tend to decrease the number of bacteria and thus the chance of infection. Whether this actually applies to the special conditions of the clinical use of these mercurials should be the subject of carefully controlled experimentation and not of *a priori* arguments. So far the proof does not fully satisfy the standards of scientific criticism.

It could also be argued, or hoped, that the mercury inhibition of growth would impair the infectivity of the bacteria, perhaps irreversibly. This too should be the subject not of argumentation but of experimental verification. This is the chief purpose of the present report, and the answer under the conditions of the experiment reported is in the negative: Bacterial cultures which have been exposed for ten or even fifteen minutes to the full commercial concentration of three of the most widely used organic mercurial agents produce fatal bacteremia when injected intraperitoneally into mice. The tests were made with a non-sporulating organism, a virulent hemolytic streptococcus "pathogenic for man and mouse," and the results are decisive. Whether other infectious agents would differ and lose their virulence when exposed to mercury may well be investigated. Actually, in other experiments in the same laboratory it has been found that the infection of laboratory animals by influenza virus may be prevented by their exposure to "mercurochrome," "merodiccine," "metaphen" and phenyl mercuric nitrate; "merthiolate" was ineffective. Others have reported the effectiveness of "mercurochrome" in inactivating *in vitro* the virus of poliomyelitis. The field of usefulness of organic mercurials should be explored, proved and defined. The proponents of these preparations should proceed seriously and diligently to this task. The Council wishes to give the necessary opportunity to meet the challenge, but it should not be deferred indefinitely. It is a field in which wishful thinking is dangerous.

AUSTIN SMITH, M.D., Secretary.



# THE BACTERIOSTATIC AND BACTERICIDAL ACTIONS OF SOME MERCURIAL COMPOUNDS ON HEMOLYTIC STREPTOCOCCI \*

In Vivo and in Vitro Studies

HARRY E. MORTON, Sc.D.

LEON L. NORTH Jr., M.D.

and

FRANK B. ENGLEJ Jr., M.S.  
Philadelphia

Mercurial compounds have been employed as disinfectants since the beginning of bacteriology. Indeed, for a long period mercurial compounds, such as bichloride of mercury, headed the list of chemicals which were thought to be effective in the killing of micro-organisms. This perhaps may be attributed to the favorable publicity which Koch<sup>1</sup> in 1881 gave to bichloride of mercury during his work with the organism causing anthrax. In substance he stated that, without special preparation of the objects to be disinfected, bichloride kills by a single application of a very dilute solution, and in a few minutes even the most resistant forms of the organisms are killed.

Geppert<sup>2</sup> in 1889 first pointed out that false inferences were drawn that bacteria were killed by the action of bichloride of mercury when growth of the organisms was prevented by traces of the chemical in the culture medium. In support of his thesis Geppert claimed that the spores of *Bacillus anthracis* were capable of infecting animals even after the spores had been treated with bichloride of mercury and produced no growth on subculturing by the usual methods. To eliminate the bacteriostatic action of the small quantity of mercury adherent to the bacteria and of the small amount of the chemical carried into the subculturing medium in the inoculum, Geppert employed ammonium sulfide to inactivate the bichloride of mercury. By this technic Geppert showed that the spores of *B. anthracis* were not killed by 1:1,000 bichloride of mercury during a period of exposure of hours, in one case as long as twenty-four hours.

In 1891 Abbott<sup>3</sup> claimed that he had confirmed Geppert's work in part, but he did not do animal experiments. In his publication in 1891, Abbott concluded, "... it is plain that for use in surgical practice the solutions of corrosive sublimate do not possess all of the advantages hitherto attributed to them."

Do other compounds of mercury possess the same shortcomings as disinfectants<sup>4</sup> as does bichloride of mercury? Are non-spore forming pathogenic micro-organisms still infectious while in a state of bacteriostasis brought about by a mercurial compound? The answers to these important questions are provided by the experimental work to be described.

From the Department of Bacteriology, University of Pennsylvania School of Medicine.

These studies have been aided by a grant from the Council on Pharmacy and Chemistry, American Medical Association.

Dr. Morton was a member of the Committee on Antiseptics and Disinfectants, American Public Health Association, 1943.

The present address of Dr. North is Philadelphia General Hospital, Philadelphia.

The present address of Mr. Engley is Camp Detrick, Frederick, Md.

1. Koch, R.: Ueber Desinfection, Mitt. a. d. k. Gesundheitsamte 1: 234-282, 1881.

2. Geppert, J.: Zur Lehre von den Antiseptics: Eine Experimental-untersuchung, Berl. klin. Wehnschr. 26: 789-794, 819-821, 1889.

3. Abbott, A. C.: Corrosive Sublimate as a Disinfectant Against *Staphylococcus Pyogenes Aureus*, Bull. Johns Hopkins Hosp. 2: 50-60, 1891.

4. Agents capable of destroying pathogenic micro-organisms and thus preventing infection.

## REASONS FOR AND MEANS OF PREVENTING THE BACTERIOSTATIC ACTION OF MERCURIAL COMPOUNDS IN GERMICIDAL TESTS

It is generally known that it is exceedingly difficult to destroy bacterial spores. Our results, about to be described, indicate that virulent hemolytic streptococci (an example of non-spore forming organisms) are still infectious after being exposed for ten minutes to any one of three organic mercurial compounds obtained in the open market. The compounds studied were (1) the disodium salt of 2,7-dibrom-4-hydroxymercurifluorescein, merbromin, N: F., "mercurochrome," (2) sodium ethylmercurithiosalicylate, "merthiolate," (3) the anhydride of 4-nitro-3 hydroxymercuri-orthocresol, "metaphen." The fact that both vegetative cells and spores are still infectious while in a state of bacteriostasis is sufficient reason for taking precautions to eliminate the bacteriostatic effect of mercury when testing mercurial compounds in vitro for germicidal activity. In the in vitro test, micro-organisms are mixed with the chemical under test and at stated intervals portions, usually a standard loopful, are transferred to an appropriate subculturing medium. It is quite generally accepted that germicides in solution bring about their action by reacting chemically with the bacterial cell. When a portion of the germicide-culture mixture is transferred into the subculturing medium, in order to determine whether the organisms are still viable some of the germicide is introduced into the subculturing medium, both free in the solution and in combination with the bacterial cells. In testing strong solutions of germicides it was realized that in some cases it was possible to carry enough of the chemical in an inoculum the size of a standard loopful into the subculturing medium to give a concentration of the germicide in the subculturing medium great enough to exert a bacteriostatic action. Shippen<sup>5</sup> in 1928 recommended transferring four loopfuls from each subculture of the culture-germicide mixture to a second tube of broth. In this way the germicide would be diluted beyond the concentration at which it would be able to exert a bacteriostatic action. By this technic he found that bichloride of mercury in a dilution of 1:200 to 1:300 failed to kill *Staphylococcus aureus* in fifteen minutes' exposure. This concentration of bichloride of mercury is three to five times as great as usually recommended and is still incapable of destroying in fifteen minutes' exposure the vegetative cells of the common pus producing organism. Mere dilution of the inoculum does not eliminate the bacteriostatic action of the mercurial contained in it. Heinemann<sup>6</sup> pointed out that dilution of the inoculum as in the Shippen technic gave falsely high killing values in several instances. This was also demonstrated by Morton<sup>7</sup> with soaps containing mercurial compounds. It has been pointed out also that dilution does not neutralize the mercury which may be bound to the bacterial cell.

Bacterial cells which have been weakened by exposure to the action of a germicide are more susceptible to the bacteriostatic action of the germicide, so it is more difficult to eliminate the bacteriostatic action of the chemical. This was pointed out by Geppert<sup>2</sup> and was

5. Shippen, L. P.: A Fallacy in the Standard Methods of Examining Disinfectants, Am. J. Pub. Health 18: 1231-1234, 1928.

6. Heinemann, B.: A Comparison of Methods Used for Evaluating the Bactericidal Properties of Mercurial Compounds, J. Am. Pharm. A. (Scient. Ed.) 32: 298-301, 1943.

7. Morton, Harry E.: "Germicidal" Soaps: I. The Importance of a Clean Skin, the Action of Soaps in Freeing the Skin of Viable Micro-organisms, and Methods for Testing the Efficiency of Germicidal (Medicated) Soaps, J. A. M. A. 124: 1195-1201 (April 22) 1944.

emphasized in one of the early textbooks on bacteriology.<sup>8</sup> For a fuller discussion of the shortcomings of mercurial compounds as disinfectants reference should be made to the report of Brewer<sup>9</sup> in 1939.

A method more reliable than mere dilution for eliminating the bacteriostatic effect of a mercurial compound in the subculturing medium during the testing for germicidal action is chemical neutralization of the mercurial. Geppert employed ammonium sulfide to inactivate the mercury in the culture-germicide mixture which was subcultured and found that the dilutions of bichloride of mercury which were germicidal were much lower than when cultured by ordinary methods. Hunt<sup>10</sup> employed hydrogen sulfide for the same purpose. The thioglycollate medium described by Brewer<sup>11</sup> in 1940 for growing micro-organisms anaerobically was also found to be capable of neutralizing the bacteriostatic action of mercurial compounds.<sup>12</sup> The National Institute of Health made this the official medium for the sterility testing of biological products beginning July 1942, and it has been subsequently modified to a slight extent (Pittman,<sup>13</sup> N. I. H. circular.<sup>14</sup>)

The objectives of our experiments were to determine (1) the effect of some of the organic mercurial compounds on an organism pathogenic for man and mouse and (2) whether the growth of the test organism in thioglycollate medium parallels infectivity for the animal body.

#### MATERIALS AND TECHNIQS

**Test Organism.**—It is desirable to select for test organisms those which are pathogenic for man as well as for some laboratory animal. We selected for this work *Streptococcus pyogenes*, strain C203M. It gave a good reaction with group A serum (Lancefield). On extract agar containing 5 to 10 per cent normal horse blood the streptococcus colonies were surrounded by large zones of hemolysis of the red blood cells. The red blood cells in blood broth were readily hemolyzed. The culture was maintained in blood extract broth composed of Bacto-beef extract 0.3 per cent, Parke-Davis peptone 1 per cent, sodium chloride 0.5 per cent and distilled water. The  $p_H$  was approximately 7.2 after sterilization. Sterile defibrinated horse blood was added to the amount of 10 per cent. Approximately 10 cc. of medium was contained in the culture tubes. Fresh subcultures were made by transferring 0.5 cc. of a previous culture to a tube of fresh medium, incubating at 37 C. for twenty-four hours, then storing in the refrigerator at 4-11 C. The stock cultures were routinely subcultured every three months. Three out of three mice were killed within sixty-five hours following the intraperitoneal injection of 1 cc. of a 1:10,000,000 ( $1 \times 10^{-7}$ ) dilution of a twenty-four hour culture. The lethal dose constituted four colonies when grown in blood extract agar.

**Experimental Animal.**—White Swiss mice weighing 17-20 Gm. each were employed.

8. Sternberg, G. M.: *A Manual of Bacteriology*, Baltimore, William Wood & Co., 1892.

9. Brewer, John H.: The Antibacterial Effects of the Organic Mercurial Compounds, with Special Reference to Their Use as Germicides for the Sterilization of Surgical and Dental Instruments, *J. A. M. A.* **112**: 2009-2018 (May 20) 1939.

10. Hunt, G. A.: The Use of Cutaneous Staphylococcus Lesions in Mice for the Evaluation of the Germicidal Activity of Disinfectants, *J. Infect. Dis.* **60**: 232-237, 1937.

11. Brewer, John H.: Clear Liquid Media for the "Aerobic" Cultivation of Anaerobes, *J. A. M. A.* **115**: 598-600 (Aug. 24) 1940.

12. Marshall, M. S.; Gunnison, J. B., and Luxen, M. P.: Test for the Sterility of Biologic Products, *Proc. Soc. Exper. Biol. & Med.* **43**: 672-673, 1940. Brewer.<sup>11</sup>

13. Pittman, M.: A Study of Fluid Thioglycollate Medium for the Sterility Test, *J. Bact.* **51**: 19-32, 1946.

14. National Institute of Health Circular: Culture Media for the Sterility Test, first revision, Jan. 15, 1945.

**Culture Mediums.**—Bacto-Anaerobe medium with dextrose, experimental, contained in each liter Proteose-peptone No. 3, Difco, 20 Gm., Bacto-beef extract 3 Gm., Bacto-yeast extract 3 Gm., malt extract, Difco, 3 Gm., dextrose 5 Gm. and agar 1 Gm. Reaction of the medium after sterilization was approximately  $p_H$  7.3.

Bacto-cooked meat medium No. 2 was a special lot for a contaminated wound project. Each liter of medium contained beef heart 454 Gm., proteose-peptone, Difco, 20 Gm., dextrose 2 Gm. and sodium chloride 5 Gm. Reaction of the medium after sterilization was approximately  $p_H$  7.4.

Bacto-tryptose phosphate broth contained in each liter Bacto-tryptose 20 Gm., Bacto-dextrose 2 Gm., sodium chloride 5 Gm. and disodium phosphate 2.5 Gm. Reaction of the medium after sterilization was approximately  $p_H$  7.3.

Hydrolyzed casein. This was received from Dr. C. M. Brewer, U. S. Department of Agriculture, who stated that it was "Trypticase-Pancreatic Digest of Casein" received from the Baltimore Biological Laboratory. A 3 per cent solution in distilled water containing 0.5 per cent sodium chloride was used. It had a reaction of  $p_H$  6.8 after sterilization.

Bacto-fluid thioglycollate medium, Linden formula, was prepared in accordance with section 4 b of the National Institute of Health Bulletin "Fluid Thioglycollate Medium for the Sterility Test," dated Dec. 30, 1941. Each liter of the medium consisted of Proteose-peptone No. 4, Difco, 30 Gm., Bacto-dextrose 5 Gm., Bacto-yeast extract 2 Gm., sodium thioglycollate, Difco, 1 Gm., Bacto-agar 0.5 Gm., sodium chloride 5 Gm., dipotassium phosphate 2.5 Gm., Bacto-methylene blue (DA-6) 0.002 Gm. and distilled water. The reaction was approximately  $p_H$  7.5 after autoclaving.

For a plating medium beef extract agar, made by adding 2 per cent agar to the beef extract broth, was used, to which was added 10 per cent sterile, defibrinated horse blood.

**Disinfectants.**—Samples of the three organic mercurial compounds "Mercurochrome," "Merthiolate" and "Metaphen" were purchased over the counter from various pharmacies and used undiluted from the original packages or diluted as for the standard phenol coefficient test.<sup>15</sup>

**Technic.**—In performing the disinfection tests, 1 cc. of a 24 hour old blood broth culture,  $\pm$  2 hours, was added to 10 cc. of the disinfectant in a test tube. After thorough mixing, 5 cc. of the culture-disinfectant mixture was transferred to an Esmarch dish to facilitate filling syringes. At intervals of five, ten and fifteen minutes 1 cc. of the culture-disinfectant mixture was removed from the test tube, 0.5 cc. inoculated into a tube containing about 11 cc. of blood broth, and the other 0.5 cc. portion inoculated into a tube containing about 11 cc. of fluid thioglycollate medium. At the ten minute interval 1 cc. portions or less, if the disinfectant was toxic for mice, of the culture-disinfectant mixture was injected intraperitoneally into white mice weighing 17-20 Gm. each. The temperature of medication was room temperature. After all subcultures had been made the tubes were thoroughly shaken and then incubated at 37 C. Subculture tubes which did not show growth were kept under observation for seven

15. Ruehle, G. L. A., and Brewer, C. M.: United States Food and Drug Administration Methods of Testing Antiseptics and Disinfectants, Circular No. 198, U. S. Dept. of Agriculture, Washington, D. C., December 1931.

days before discarding. Growth in the subculture tubes was checked microscopically and in some cases by streaking onto blood agar plates. Streptococci were demonstrated in all critical tubes. The heart's blood from some of the mice which died following the injection of each culture-germicide mixture was streaked on blood agar plates and hemolytic streptococcus colonies were demonstrated. Representative cultures isolated from the heart's blood cultures were demonstrated to be group A by the technic of Brown.<sup>16</sup>

**Controls.**—Comparable amounts of the germicides which were contained in the dose of germicide-culture mixtures were injected intraperitoneally into mice to prove that the mice were not killed by the germicide. Virulence of the culture was demonstrated by adding 1 cc. of culture to 10 cc. of sterile distilled water, allowing to stand at room temperature for ten minutes, then injecting 1 cc. into each of four mice. Hemolytic streptococci were demonstrated in the heart's blood

because the loop was unsatisfactory, and Tice and Pressman<sup>19</sup> employed 0.05 cc. amounts. The toxicity of some of the compounds did not permit us to inject mice with more than 0.1 or 0.2 cc. The volume of culture-germicide mixture transferred by means of a pipet is arbitrary. By transferring larger volumes a more critical test is placed on the germicide, but this should not present an obstacle if the compound is an effective germicide.

#### EXPERIMENTAL

It would be very advantageous if cultures of virulent hemolytic streptococci could be grown in a blood-free culture medium with virulence of the culture maintained. The culture of hemolytic streptococcus strain C203M, recently passed through mice, was inoculated into the following five mediums: (1) extract broth containing 10 per cent horse blood, (2) Bacto-anaerobe medium, experimental, (3) Bacto-cooked meat medium, (4) Bacto-tryptose phosphate broth and (5) hydro-

TABLE 1.—The Number of Hemolytic Streptococci Present in Twenty-Four Hour Cultures in Various Culture Mediums and the Virulence of the Streptococci for White Mice

Dilution of culture.....	10 <sup>-3</sup>	10 <sup>-4</sup>	10 <sup>-5</sup>	10 <sup>-6</sup>	10 <sup>-7</sup>
Med.um.....		Extract broth + 10 per cent horse blood			
Number of colonies.....	(47,000)*	(4,700)*	(470)*	47	4
Three mice injected with each dilution.....	Died 20 hrs. Died 20 hrs. Died 20 hrs.	Died 20 hrs. Died 22 hrs. Died 22 hrs.	Died 22 hrs. Died 22 hrs. Died 22 hrs.	Died 65 hrs. Died 65 hrs. Died 65 hrs.	Died 65 hrs. Died 65 hrs. Died 65 hrs.
Number of colonies.....	(26,000)*	Bacto anaerobe medium with dextrose, experimental (2,600)*	Est. 200	20	7
Three mice injected with each dilution.....	Died 20 hrs. Died 20 hrs. Died 22 hrs.	Died 65 hrs. Died 65 hrs. Died 65 hrs.	Died 22 hrs. Died 65 hrs. Died 120 hrs.	Died 65 hrs. Died 65 hrs. Died 65 hrs.	Died 65 hrs. Survived Survived
Number of colonies.....	(57,000)*	Bacto-cooked meat medium number 2, experimental (5,700)*	(5.0)*	57	4
Three mice injected with each dilution.....	Died 20 hrs. Died 22 hrs. Survived	Died 65 hrs. Died 65 hrs. Died 65 hrs.	Died 65 hrs. Died 72 hrs. Survived	Died 65 hrs. Survived Survived	Survived Survived Survived
Number of colonies.....	(19,700)*	Bacto-tryptose phosphate broth (1,970)*	197	20	3
Three mice injected with each dilution.....	Died 65 hrs. Died 65 hrs. Died 65 hrs.	Died 65 hrs. Survived Survived	Died 65 hrs. Died 7 days Survived	Died 72 hrs. Died 72 hrs. Survived	Survived Survived Survived
Number of colonies.....	120	Hydrolyzed casein medium 12	1	0	0
Three mice injected with each dilution.....	Died 65 hrs. Survived Survived	Died 65 hrs. Died 72 hrs. Died 8 days	Survived Survived Survived	Survived Survived Survived	Survived Survived Survived

\* Colonies too numerous to count. Number estimated from colony count of plate with high dilution of inoculum. Survived = mice alive and healthy at end of eight days, when experiment was terminated.

after death of the mice. Representative cultures isolated from the heart's blood of the dead mice were demonstrated to be group A by the technic of Brown.<sup>16</sup>

The transferring of a measured amount of culture-germicide mixture to the subculture tubes and to mice differed from the standard technic of transferring one loopful, but we feel that it is desirable and advantageous. The standard loop is estimated to hold about 0.02 cc. By transferring a larger volume one has a better chance of transferring viable organisms if they exist in the culture-germicide mixture. This is desirable, as our results indicate that a minimum of four streptococcus organisms of the strain used were required to produce a fatal infection in mice. Garrod<sup>17</sup> in 1935 pointed out that "an adequately large number of bacteria should be added to cultures in which bacteriostatic action is being studied." We found that a volume of 0.5 cc. could be employed conveniently in our in vitro tests. Tobie and Orr<sup>18</sup> transferred inoculums of 0.02 cc. with pipets

lyzed casein medium. Serial transfers were carried through the mediums until the cultures had been grown in each medium for nineteen successive transfers. A

TABLE 2.—Comparison of Two Culture Mediums, with Modifications for Their Ability to Support Growth of Hemolytic Streptococci

One medium capable of neutralizing the bacteriostatic action of mercurial compounds and one medium incapable of such action

Dilution of inoculum.....	10 <sup>-5</sup>	10 <sup>-6</sup>	10 <sup>-7</sup>	10 <sup>-8</sup>	10 <sup>-9</sup>	10 <sup>-10</sup>
Number of colonies developing from an inoculum of 0.5 cc.....	..	..	11	2	0	..
Estimated number of organisms in inoculum.....	1,100	110	11	1 or 2	1 or 0	..
Beef extract broth.....	+	+	+	+	+	+
Beef extract broth + 10 per cent blood..	+	+	+	+	+	+
Beef extract broth + 0.5 per cent glucose	+	+	+	+	+	+
Beef extract broth + 0.2 per cent cerulose	+	+	+	+	+	+
Beef extract broth + 10 per cent blood + 0.2 per cent cerulose.....	+	+	+	+	+	+
Bacto-thioglycollate medium, Linden's formula .....	+	+	+	+	+	+

sixth medium, Bacto-thioglycollate medium, Brewer's formula, was also included, but contamination of the culture caused us to drop that medium from the series.

16. Brown, J. Howard: A Simplified Method for Grouping Hemolytic Streptococci by the Precipitin Reaction, J. A. M. A. 111: 310-311 (July 23) 1936.

17. Garrod, L. P.: The Effect of Bacterial Numbers on Minimum Bacteriostatic Concentrations, J. Infect. Dis. 57: 247-251, 1935.

18. Tobie, W. C., and Orr, M. L.: Determination of Phenol Coefficients in Presence of Surface Tension Depressants, J. Lab. & Clin. Med. 29: 767-768 (July) 1944.

19. Tice, L. F., and Pressman, R.: Antiseptics of the Quaternary Ammonium Type in the Presence of Positive and Negative Gelatin, J. Am. Pharm. A. (Sc. Ed.) 34: 201-204 (Aug.) 1945.



When the growths in the nineteenth serial transfers in each medium were 24 hours old, serial dilutions of each culture were made in extract broth. One cc. of each dilution was inoculated intraperitoneally into each of 3 mice, and 1 cc. was made into a blood agar poured plate. The results are summarized in table 1.

The results summarized in table 1 indicate that extract broth containing 10 per cent horse blood satisfactorily supported growth of the hemolytic streptococci and the organisms possessed the highest virulence for mice. Mediums not containing blood were not as satisfactory.

For the work to be described it is necessary to have two culture mediums which will support growth of hemolytic streptococci equally well. One of the culture mediums must be capable of neutralizing the bacteriostatic action of mercurial compounds, and for this

ten minutes was not a disinfectant because mice injected with such mixtures invariably died. In all 16 out of 17 mice injected with such mixtures died. Mercurochrome 2 per cent and metaphen 1:500 failed to kill streptococci within an exposure period of even fifteen minutes when the culture-germicide mixtures were subcultured into thioglycollate medium, and they failed to protect all of the mice from fatal infections. When the cultures of streptococci were treated with the marketed concentrations of these compounds diluted 1:2 and then injected into mice nearly all of the mice died. Perhaps the reason that growth of the streptococci in the thioglycollate subculturing medium was not accompanied with killing of all the animals is that fewer organisms are needed to initiate growth in the culture medium than are needed to kill a mouse. This is evident from the data in tables 1 and 2.

TABLE 3.—Results\* Obtained When Various Compounds Were Injected into Mice

And when mixtures of streptococci and these compounds were subcultured into blood broth and thioglycollate medium after intervals of exposure of 5, 10, and 15 minutes and the culture germicide mixture injected into mice after an exposure of ten minutes

Material	Dilution	Blood Broth, Minutes			Thioglycollate Medium, Minutes			Number of Mice Injected	Amount Injected	Results
		5	10	15	5	10	15			
Mercurochrome 2 per cent	Undiluted	..	..	..	..	..	..	4	0.1 cc.	3 survived, 1 died 68 hours.
Mercurochrome 2 per cent	1:2	..	..	..	..	..	..	4	0.1 cc.	All survived.
Mercurochrome 2 per cent	Undiluted	—	—	—	+	+	+	4	0.1 cc.	1 died <15 hours, gram negative rod isolated from heart's blood. 1 died <15 hours, spreader isolated from heart's blood. 1 died 25 hours, no hemolytic streptococci isolated from heart's blood. 1 died 40 hours, hemolytic streptococci isolated from heart's blood.
Mercurochrome 2 per cent	1:2	—	—	—	+	+	+	4	0.1 cc.	All died <40 hours. Hemolytic streptococci isolated from heart's blood of all of the mice.
Metaphen 1:500.....	Undiluted	..	..	..	..	..	..	4	0.1 cc.	All survived.
Metaphen 1:500.....	1:2	..	..	..	..	..	..	4	0.2 cc.	All survived.
Metaphen 1:500.....	Undiluted	—	—	—	+	+	+	4	0.1 cc.	2 survived, 2 died. Heart's blood of 1 mouse cultured and hemolytic streptococci found.
Metaphen 1:500.....	1:2	—	—	—	+	+	+	4	0.2 cc.	1 died 25 hours. 2 died <40 hours. Hemolytic streptococci in the heart's blood. 1 survived.
Merthiolate 1:1,000.....	Undiluted	..	..	..	..	..	..	2	1 cc.	All survived.
Merthiolate 1:1,000.....	1:2	..	..	..	..	..	..	2	1 cc.	All survived.
Merthiolate 1:1,000.....	Undiluted	—	—	—	+	+	+	4	0.5 cc.	All died in 24 hours. Heart's blood of 2 mice cultured and hemolytic streptococci in both.
Merthiolate 1:1,000.....	1:2	—	—	—	+	+	+	4	0.6 cc.	3 died in 24 hours. 1 died in 48 hours. Heart's blood of 1 mouse cultured and hemolytic streptococci found.
Phenol 1:50.....	.....	..	..	..	..	..	..	4	0.5 cc.	All survived.
Phenol 1:50.....	.....	—	—	—	—	—	—	4	0.5 cc.	3 survived, 1 died ½ hour from trauma during injection.
Phenol 1:100.....	.....	—	—	—	+	—	—	4	0.5 cc.	All survived.
Phenol 1:120.....	.....	—	—	—	+	+	+	4	0.5 cc.	All survived.
Phenol 1:140.....	.....	—	—	—	+	+	+	4	0.5 cc.	1 died 24 hours; 2 died <41 hours. Hemolytic streptococci isolated from heart's blood of all 3 mice. 1 survived.

\* These results are from one experiment but are typical of the results usually obtained in the various tests which were made.  
— = no growth; + = growth of the test organism. .. = toxicity test on disinfectants.

medium we selected Bacto-thioglycollate medium, Linden's formula. The other medium must be incapable of neutralizing such bacteriostatic action, and beef extract broth with the addition of various substances was tried. The results are summarized in table 2.

From the results summarized in table 2, beef extract broth containing 10 per cent horse blood supported growth of hemolytic streptococci C203M as well as did Bacto-thioglycollate medium, Linden's formula. The addition of 10 per cent blood to the extract broth was preferred to 0.2 per cent cerulose because of the ease of reading growth in the medium containing blood and because it is the medium in which the organisms are maintained in culture.

Typical results obtained from numerous experiments wherein the cultures of hemolytic streptococci were exposed to the action of the various compounds and then subcultured and also injected into mice are given in table 3. It can be seen that, if subculturing of the mercurial germicide-culture mixture into thioglycollate medium resulted in growth of the culture, the organisms are still capable of producing a fatal infection in the animal body. Merthiolate 1:1,000, aqueous, when allowed to act on a culture of hemolytic streptococci for

#### COMMENT

In a preliminary report of this work<sup>20</sup> we made the statement that metaphen 1:500 was germicidal in an exposure of ten minutes but not of five minutes. These results were obtained when the culture-germicide mixture was subcultured to blood broth and at the end of the experiment transfers were made from each subculture blood broth tube to a second tube of blood broth and to a tube of thioglycollate medium. The subculturing from the primary subculture tubes, as recommended by Shippen,<sup>5</sup> does not give results as reliable as when the subcultures are made directly into a medium which will neutralize the bacteriostatic action of the mercurial compound as recommended by Brewer<sup>11</sup> and as required by the National Institute of Health<sup>14</sup> in the sterility testing of biologic products. In this particular experiment only 1 out of 4 mice injected with the mixture of culture and metaphen 1:500 died, but in another experiment 2 out of 4 animals died. The marketed solution of a germicide should be more effective in destroying pathogenic organisms.

20. Morton, H. E.; North, L. L., and Engley, F. B., Jr.: *In Vitro and In Vivo Studies on the Bacteriostatic and Bactericidal Actions of Mercurial Disinfectants on Hemolytic Streptococci*, J. Bact. 50: 125-126 (July) 1945.

Johnson and Meleney<sup>21</sup> reported that merthiolate was ineffective in preventing contamination of blood plasma, and Morgan, Simmons and Biggs<sup>22</sup> observed that organisms exposed to a concentration of 1:1,000 merthiolate for seven days at 5 C. proved viable when subcultured to thioglycollate medium. The longest period of exposure of hemolytic streptococci to merthiolate 1:1,000 was fifteen minutes at room temperature, and we always found the cultures viable when subcultured in thioglycollate medium. Although Graydon and Biggs<sup>23</sup> reported that the lag period may extend to weeks or even months when organisms are treated with sublethal doses of antiseptic, such as merthiolate, we observed no change in our subculture tubes between the second and sixth days of incubation, so terminated our observations on the sixth day. The results obtained within that period were obvious and satisfied the purpose of our experiment.

Finding that the marketed solutions of mercurochrome, metaphen and merthiolate failed to kill all the vegetative cells in a culture of hemolytic streptococci in vitro is not surprising in view of the results published by Hoyt, Fisk and Burde<sup>24</sup> and Nye.<sup>25</sup> It was to be expected that Green and Birkeland<sup>26</sup> would fail to find any therapeutic action when merthiolate (1:10,000 to 1:30,000) and metaphen (1:5,000 to 1:20,000) were applied to the chorioallantoic membranes inoculated with *Staphylococcus aureus*. In working with metaphen, mercurial M, merthiolate, mercurochrome and bichloride of mercury, Smith, Czarnetzky and Mudd<sup>27</sup> came to the conclusion that the activity of a mercurial antiseptic in serum is reduced to 0.33 to 0.007 per cent of its activity in saline solution. The marketed solutions of the three mercurials studied did not completely kill cultures of hemolytic streptococci in distilled water in an exposure of ten minutes, so any further reduction in antibacterial activity by the presence of serum would not leave much to be expected in the way of germicidal action. In spite of these facts the label on a bottle of "Solution Merthiolate, 1:1,000, Stainless" purchased as recent as June 1947 states that it is "a stable, stainless, organic mercury compound solution of high germicidal value, particularly in serum and other protein media." It is not highly germicidal and especially does not possess high germicidal value in the presence of serum and other protein mediums. The loss of antibacterial activity of mercurials in the presence of serum proves their incompatibility with serum. Not only is the antibacterial action of mercurial compounds much reduced in the presence of blood serum, but Waller<sup>28</sup> has found that a final concentration of 1:5,000 merthiolate destroyed the anti-Rh agglutinins in human serums.

The comparative in vitro studies of mercurochrome, metaphen and merthiolate on embryonic tissue cells and bacterial cells by Salle and Lazarus<sup>29</sup> cannot be ignored. These investigators found that metaphen, merthiolate and mercurochrome were 12, 35 and 262 times respectively more toxic for embryonic tissue cells than for *Staphylococcus aureus*. Nye<sup>25</sup> and Welch<sup>30</sup> also found the same three mercurial compounds more toxic for leukocytes than for bacterial cells. Not only is there the direct toxic action of the mercurial compounds on the cellular and humoral components of the animal body, but there is also the possibility of sensitization. Hollander<sup>31</sup> has recently reported a case of contact dermatitis produced by tincture of merthiolate.

We wished to learn whether organisms put in a state of bacteriostasis by a mercurial compound were harmless if introduced into the animal body. It is quite obvious that they are not harmless. There is a good correlation between the growth of hemolytic streptococci in thioglycollate medium and fatal septicemia in mice. In view of our recent knowledge of disinfectants, we wished to learn what might be expected of the three most commonly advertised mercurial compounds. The marketed aqueous solutions of the three compounds mercurochrome, merthiolate and metaphen are not effective disinfectants because when virulent organisms are treated with the substances for as long as ten minutes and introduced into the animal body either intraperitoneally or intradermally, the animals are not protected from infection. The substances are not effective germicides, as cultures treated with them are still viable. Neither are the substances effective antiseptics, as they are incapable of preventing sepsis when the pathogenic organisms are exposed as long as ten minutes to the substances. It can be stated that the substances have a bacteriostatic action. The efficacy of employing a bacteriostatic agent for topical application is beyond the scope of this paper. We only wish to point out that a pathogenic organism placed in a state of bacteriostasis by a mercurial compound is still capable of producing a fatal septicemia if introduced into the animal body and capable of producing a localized infection if introduced into the skin.<sup>10</sup>

#### SUMMARY

The organomercurial compounds "mercurochrome," "merthiolate" and "metaphen," as supplied in aqueous solutions on the market, possess many shortcomings as disinfectants. Aqueous solutions of these compounds may not completely kill cultures of virulent hemolytic streptococci, in that mice receiving an intraperitoneal injection of the culture-germicide mixture, after ten minutes' exposure of the organisms to the drugs, usually die, and hemolytic streptococci can be isolated from the heart's blood after death of the mice.

Hemolytic streptococci, an example of non-spore forming pathogenic organisms, while in a state of bacteriostasis produced by a mercurial compound, are still infectious for the animal body. Bactericidal rather than bacteriostatic action of the compounds is necessary to prevent a generalized infection.

Reports in the literature indicate that these three organomercurial compounds are more toxic for embryonic tissue cells and leukocytes than for bacterial cells.

21. Johnson, B., and Meleney, F. L.: Blood Substitutes and Blood Transfusion, edited by Stuart Mudd and William Thalheimer, Springfield, Ill., Charles C Thomas, 1942, p. 263.

22. Morgan, F. G.; Simmons, R. T., and Biggs, C. L.: Pooled Human Serum: A Note on Testing for Sterility in the Presence of Certain Antiseptics, *M. J. Australia* **11**: 515-517 (Dec. 12) 1942.

23. Graydon, J. J., and Biggs, C. L.: Some Factors Influencing Bacterial Survival in the Presence of Antiseptics, *M. J. Australia* **11**: 513-515 (Dec.) 1942.

24. Hoyt, A.; Fisk, R. T., and Burde, G.: The Antibacterial Action of Certain Disinfectants, *Surgery* **12**: 786-790 (Nov.) 1942.

25. Nye, R. N.: The Relative In Vitro Activity of Certain Antiseptics in Aqueous Solution, *J. A. M. A.* **108**: 280-287 (Jan. 23) 1937.

26. Green, T. W., and Birkeland, J. M.: The Use of the Developing Chick Embryo as a Method of Testing the Antibacterial Effectiveness of Wound Disinfectants, *J. Infect. Dis.* **74**: 32-36 (Jan.-Feb.) 1944. Nye.<sup>25</sup>

27. Smith, D. C.; Czarnetzky, E. J., and Mudd, Stuart: The Mechanism of Inactivation of Mercurial Antiseptics by Serum and Its Implications Regarding the Possibilities of Intravenous Antiseptics, *Am. J. M. Sc.* **192**: 790-808 (Dec.) 1938.

28. Waller, R. K.: The Action of Sodium Ethylmercurithiosalicylate on Human Anti-Rh Serum, *Am. J. Clin. Path. (Tech. Supp.)* **8**: 116-117, 1944.

29. Salle, A. J., and Lazarus, A. S.: A Comparison of the Resistance of Bacteria and Embryonic Tissue to Germicidal Substances: I. Merthiolate, *Proc. Soc. Exper. Biol. & Med.* **32**: 665-667 (Feb.) 1935; II. Metaphen, pp. 937-938; III. Mercurochrome, pp. 1057-1060.

30. Welch, H.: Mechanism of the Toxic Action of Germicides on Whole Blood Measured by the Loss of Phagocytic Activity of Leukocytes, *J. Immunol.* **37**: 525-533, 1939.

31. Hollander, L.: Contact Dermatitis Produced by Tincture of Merthiolate, *Arch. Dermat. & Syph.* **50**: 123 (Aug.) 1944.

## Inactivation of Nutrients by Heating\* With Glucose<sup>1</sup>

A. R. PATTON and E. G. HILL

Chemistry Department,  
Colorado A & M College, Fort Collins

Hill and Patton (1) found that the slight discoloration occurring during the autoclaving of media for the microbiological assay for L-tryptophan was caused by interaction with glucose, resulting in decreased growth of *Streptococcus faecalis* R. It was not known at that time whether the poorer growth resulted from destruction of nutrients or formation of growth inhibitors as products of the browning reaction. The work reported here indicates that the decreased growth is due to destruction of nutrients.

TABLE 1  
LOSS OF L-TRYPTOPHAN DUE TO INTERACTION  
WITH GLUCOSE

Treatment	Browning (% T/610)	Hydroxymethyl- furfural (%)	tryptophan loss (%)
Unheated .....	100	0	0
Heated .....	81.5	0.52	60
Heated at pH 10 ..	41.5	2.25	26

It is known that the browning reaction is promoted by alkalinity, and that hydroxymethylfurfural is one of the chief reaction products. Advantage was taken of these facts in the following tests: Aliquots of a solution containing known amounts of L-tryptophan and D-glucose were heated under suitable conditions to cause browning similar in appearance to that which occurred during autoclaving of media. The extent of browning was measured by determining the decrease in transmission at 610 mμ in a Coleman spectrophotometer. Hydroxymethylfurfural content, used as an indicator of the concentration of browning reaction products, was estimated from the absorption increase at 284 mμ in a Beckman DU spectrophotometer. The loss of L-tryptophan resulting from the browning reaction was determined by microbiological assay using the sucrose medium to prevent further browning loss. Aliquots buffered at pH 10 were prepared to obtain samples in which browning was only partially due to interaction with tryptophan. These mixtures produced more browning in less time. Growth of *Str. faecalis* R was measured turbidimetrically after 16 hrs by decrease in transmission at 610 mμ. At the dilutions used for assay, the browned samples were colorless at this wave length.

As shown in Table 1, better growth was obtained from the tryptophan-glucose sample heated at pH 10, in spite of the fact that more browning occurred and more hydroxymethylfurfural was formed. On the other hand, the solution containing only glucose and tryptophan,

showing less browning and much less hydroxymethylfurfural formation although heated for a longer time, permitted poorer growth. These data indicate that decrease in growth was due not to formation of growth inhibitors as products of the browning reaction but to actual destruction of part of the tryptophan.

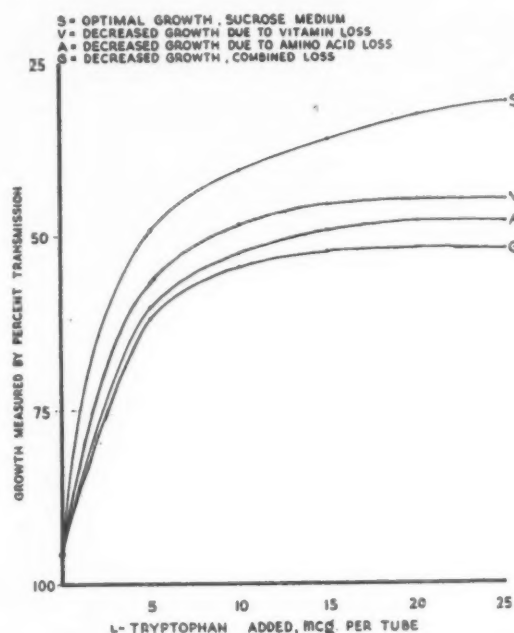


FIG. 1. Growth of *Str. faecalis* R in standard series for L-tryptophan assay, showing decreased growth due to autoclaving in presence of glucose.

It also appears that such destruction is not limited to tryptophan. Both L-lysine and DL-methionine, upon heating in the presence of glucose, underwent similar destruction, as determined by subsequent microbiological assay using synthetic amino acid media. Curve G (Fig. 1), which is a standard growth curve for L-tryptophan as obtained by the customary assay method using glucose in the medium, shows the total growth-decreasing effect of the browning reaction. Curve V resulted from the addition of a pure sterile solution of the amino acids to the autoclaved medium before inoculating, in an attempt to reveal the extent of vitamin destruction during autoclaving. Similarly, to produce curve A the vitamins were replaced after autoclaving, to show the extent of amino acid destruction. These curves indicate that nutrients in both the vitamin class and the amino acid class suffered damage during autoclaving with glucose. The vitamins required in the medium (B complex) contain nitrogenous moieties which might conceivably react with glucose similarly to amino acids. Inactivation of nutrients was minimized by using sucrose instead of glucose in the medium (Curve S), as previously described by the authors (1).

### Reference

- HILL, E. G., and PATTON, A. R. *Science*, 1947, **105**, 481.

<sup>1</sup> Scientific Series No. 253, Colorado A & M College Experiment Station.



# Therapeutic Trends

New Trends in Medicine and Pharmacy Include TEROPTERIN AND DIOPTERIN TO RELIEVE CANCER PAIN - BENADRYL USED TO TREAT COMMON COLD - COLLOIDAL IRON HYDROXIDE IN THE TREATMENT OF HYPOCHROMIC ANEMIA - BAL-INTRAV IN ARSENICAL POISONING

## TEROPTERIN AND DIOPTERIN USED TO RELIEVE CANCER PAIN

Experimental use of two chemical compounds related to folic acid to relieve pain in cancer in man has been reported in *Science* (December 19, 1947). This preliminary study reveals that these compounds, pteroyltriglutamic acid (teropterin) and pteroyldiglutamic acid (diopterin) are non-toxic and may be administered with ease by either the intravenous or intramuscular route.

The authors emphasize the fact that these new substances should not be employed in the routine therapy of patients with cancer but the experiments indicate that further investigation of the action of teropterin and diopterin and related compounds would be of interest.

In the early experimental work it was reported that a folic acid concentrate and a fermentation L. casei factor inhibited growth of sarcoma in mice. At that time it was believed that this substance was folic acid (pteroylglytamic acid) but subsequent work showed that it was pteroyltriglutamic acid, a conjugate of folic acid. Later studies also showed that folic acid was not effective in producing regression of breast cancers.

Pteroyltriglutamic acid and pteroyldiglutamic acid were synthesized and used in the treatment of 90 patients with malignant disease. Toxicity, dosage, method of administration and certain general effects were noted. More detailed chemical and pathological studies will be reported



later. Teropterin and diopterin are available from Lederle Laboratories for investigational use only.

## BENADRYL USED TO TREAT COMMON COLD

Symptoms of the common cold have been controlled experimentally with the antihistamine drug, benadryl. According to a report in the *U.S. Naval Medical Bulletin* (September-October 1947), benadryl has been used to treat more than 100 cases with encouraging results. In the clinical work it was found that benadryl therapy completely aborted 10 per cent of the cases treated and it shortened the course and afforded marked subjective relief to 95 per cent of all cases.

Use of benadryl for colds was first suggested when it seemed to have a palliative effect upon a patient with an alimentary form of allergy, for which he was being treated with benadryl. Since it is believed that many of the so-called common colds have an allergic origin or at least an allergic factor, and from the experience of this first patient it was decided to use benadryl routinely in all cases of common colds. From the experience gained in this experimental work it was found that the following properties of benadryl make it useful in treatment of the common cold: (1) It markedly inhibits the serous discharge from the respiratory mucous membranes to a degree equal to that of a conservative dose of atropine. (2) Produces a sedative effect equal to a therapeutic dose of phenobarbital in the majority of cases. The sleep thus induced is usually dreamless and thoroughly refreshing.

The author believes that a large proportion of the cases of the common cold, virus in origin, could be aborted by early and prompt treatment with benadryl. In this study 50 mg. capsules were administered to adults and 10 to 25 mg. capsules to children. No untoward actions were noted but patients should be warned of the soporific effect of benadryl and cautioned to avoid driving a car or operating potentially dangerous machinery while taking the drug.

In conclusion the author states that benadryl has proved to be the most satisfying single therapeutic agent for the treatment of the common cold.

#### COLLOIDAL IRON HYDROXIDE IN THE TREATMENT OF HYPOCHROMIC ANEMIA

Colloidal iron hydroxide is an effective preparation for the treatment of hypochromic anemia according to a report in The American Journal of Medical Sciences (September 1947). This preparation satisfies all the requirements desired for iron therapy including: (1) An effective hematopoietic response with small amounts, i.e., a high index of utilization; (2) A readily available form for solubility and for action with gastric hydrochloric acid; and (3) A low factor of irritability by virtue of its chemical nature and by the small amounts required for good hemoglobin. Another advantage in using colloidal iron hydroxide in preference to other iron preparations is the fact that iron hydroxide, combined with protein, is a normal constituent of foodstuffs and therefore, is more readily utilized. The colloidal nature of this preparation offers a greater surface area for chemical action with the intestinal contents, thus facilitating alteration to the ferrous state.

In a study to select an iron preparation which is effective and well tolerated by the patient, two phases of the problem were considered. First, in determining the utilization of iron when administered orally as colloidal ferric hydroxide it was found that its daily iron utilization, although equivalent to ferrous sulfate, is achieved with smaller doses. Secondly, a study was made to evaluate the incidence of gastrointestinal irritation resulting from the use of colloidal iron hydroxide as compared with ferrous sulfate. A series of patients were administered either colloidal iron hydroxide or ferrous sulfate and after a suitable rest period the other drug was administered and followed according to the same regimen. Summarizing the results, the authors state that the usual dose of ferrous sulfate produced approximately twice the incidence of gastrointestinal irritation as compared with an equivalent dose of colloidal iron hydroxide. Constipation was the most frequent untoward action. Vomiting and abdominal colic were not noted with the colloidal preparation. Furthermore, the severity of the gastrointestinal irritation was less and its occurrence more transitory when colloidal iron hydroxide was administered and many patients unable to tolerate ferrous sulfate have experienced little difficulty with colloidal iron hydroxide.

#### BAL-INTRAV IN ARSENICAL POISONING

BAL-INTRAV, which is a glucoside of 2, 3-dimercaptopropanol, has been shown to be non-toxic as an intravenous injection in arsenical poisoning. Studies of the biological and chemical properties including toxicity tests on a series of thiols were described in The Biochemical Journal, London, (Vol. 41, No. 3).

Earlier reports have evaluated BAL (2,3-dimercaptopropanol) as an antidote in arsenical poisoning. When applied to the skin it provides a considerable measure of protection against the vesicant action of lewisite, but as an antidote in systemic poisoning, BAL has the disadvantage of being of rather high toxicity. Therefore, it cannot be administered by injection in large amounts.

In view of the aforementioned facts, a number of thiol acids were prepared and toxicity studies were made using BAL, mercaptoacetate, mercaptosuccinate, mercaptoadipate, acetylmercaptosuccinate, dimercaptodipate, glutathione, glutathione and the BAL glucoside. Intravenous injections were given to rats and toxic effects noted. The most effective therapeutic action was obtained with BAL-INTRAV which prevented death in 100 per cent of the animals studied even if not given until several hours after administration of a lethal dose of lewisite.

This preparation is not to be confused with BAL-in-oil which cannot be given intravenously,

#### TETRAETHYLAMMONIUM CHLORIDE IN TREATING ULCERS

Tetraethylammonium chloride which is now available as "Etamon" may also prove effective in the treatment of duodenal ulcers according to a report in Science (November 7, 1947). This drug is an autonomic blocking agent which has been found useful in the treatment of patients suffering from peripheral vascular diseases and other blood diseases characterized by vasospasm. Since vagotomy (cutting of the vagus nerve) has been reported effective in preventing gastric ulceration and since tetraethylammonium chloride blocks the impulses at the autonomic ganglia, it was believed that it might prove useful in treating ulcers.

This study was suggested when it was noted that a hypertensive patient who also had a duodenal ulcer was relieved of ulcer pain after a single intramuscular injection of 1.2 grams of tetraethylammonium chloride. Cessation of gastrointestinal motility, a decrease in the acidity and volume of the gastric juice as well as relief of pain resulted.

# Timely Drugs

EDITED BY  
ALBERT L. PICCHIONI, PHARMACIST  
UNIVERSITY HOSPITAL, ANN ARBOR, MICHIGAN

HEPARIN IN PITKIN'S MENSTRUUM -  
FURACIN SOLUTION - THEPHORIN - BENZE-  
DRINE AND DEXEDRINE IN NEW DOSAGE  
FORMS - ARE DRUGS OF TIMELY INTEREST  
TO THE HOSPITAL PHARMACIST.

HEPARIN IN PITKIN MENSTRUUM . . . which provides a slower and more equable distribution of heparin is now available for use in the prophylaxis and treatment of thromboembolic diseases.

Some disadvantages encountered with the use of the usual aqueous solutions of heparin are: the cumbersome method of administration which consists of repeated daily intravenous injections or the continuous drip procedure; the expense involved as a result of the huge amount of drug required, and the restriction of motion of the patient.

The heparin in Pitkin menstruum, which is administered subcutaneously, was introduced in an attempt to regulate the release of heparin. Through its use, elevation of blood-clotting time is achieved for periods of 24 to 48 hours instead of three to four hours. And the cost to the patient is estimated to be 1/5 to 1/6 that which follows the use of the aqueous solution of heparin.

Pitkin's menstruum is composed of the following ingredients:

Gelatin	15 to 30%
Dextrose	5 to 12%
Glacial Acetic Acid	0.5%
Distilled Water, sufficient to make	100%

The rate of release of heparin is dependent upon the viscosity of the menstruum. A concentration of 18 per cent gelatin and 8 per cent dextrose is considered by some investigators to produce the best results.

Heparin in Pitkin's menstruum is available with or without vasoconstrictor drugs. The presence of the latter is said to prolong the anticoagulant action of heparin, and their presence is especially desirable in the treatment of thromboembolic venous disease. However, it is advisable to use heparin in Pitkin menstruum without vasoconstrictor drugs in the treatment of thromboembolic arterial disease in order to avoid the possible complication of arterial spasm. Their presence may also be contraindicated in hypertensive patients or in those with myocardial disease.

The dosage of heparin in Pitkin menstruum recommended in thromboembolic arterial disease is 400 mg. every other day until patency of the blood vessel is restored. In thrombophlebitis and/or phlebothrombosis 300 mg. is considered an effective initial dose. This amount is repeated every other day for a period of one to two weeks. For prophylactic use a dosage of 200 mg. to 300 mg. administered every alternate day has been used.

Heparin in Pitkin menstruum should be used subcutaneously, never intravenously. Intragluteal administration may be employed but absorption may be too rapid. Since digitalis inhibits the anticoagulant action of heparin it is advisable to avoid the use of this drug during periods of heparinization.

Heparin in Pitkin menstruum is obtainable from William R. Warner and Company in 2 cc. and 3 cc. ampules containing 200 mg. and 300 mg. of heparin respectively. They are available with or without vasoconstrictors. Any desired dose of heparin, with or without vasoconstrictor drugs, can be given by combining the contents of two or more ampules. The 2 cc. ampules contain 12.5 mg. of ephedrine sulfate and 0.5 mg. of epinephrine hydrochloride per cc. as vasoconstrictors. The 3 cc. ampules contain 8.3 mg. of the former and 0.33 mg. of the latter per cc.

FURACIN SOLUTION . . . now being marketed by Eaton Laboratories, represents another preparation involving the use of the nitrofurantoin compound furacin—a new type of chemotherapeutic agent, possessing both bactericidal and bacteriostatic properties.

Furacin solution is recommended for use in conditions where the furacin soluble dressing preparation is inconvenient, such as on wet dressings where the gauze dressings on infected wounds and burns are to be kept moist. When used on wet dressings furacin solution also has the advantage that the dressings do not dry out as rapidly as when purely aqueous solutions are used.

Furacin solution consists of the following



## formula:

Furacin (5, nitro-2-furaldehyde semi-carbazone)	0.2%
Wetting Agent (polyethylene glycol of moniso-octyl phenyl ether)	0.3%
Carbowax	65.0%
Water	34.5%

This formula, except for the presence of water and the wetting agent, is similar to the one for furacin soluble dressing, which has the same concentration of furacin. The antibacterial activity of the two preparations is the same.

Furacin solution will dissolve readily in wound exudates as it is miscible with organic matter such as pus, blood, and serum. The presence of the wetting agent in the solution reduces surface tension and, thereby, aids the solution to penetrate small fissures.

Furacin solution is available in 4 ounce and 16 ounce bottles. It will become decolorized upon exposure to light and should, therefore, be dispensed in dark bottles.

**THEPHORIN** . . . an antihistamine drug has recently been released by Hoffman-La Roche and is available as 25 mg. tablets or as a syrup containing 10 mg. per teaspoonful. Thephorin is useful in the treatment of allergic disorders, such as hay fever, urticaria, allergic skin diseases and drug reactions, some cases of asthma, and other allergic complaints. It shows a low incidence of side reactions and is not likely to cause drowsiness.

Use of thephorin experimentally in dermatoses in which histamine was thought to produce symptoms is reported in The Journal of Investigative Dermatology (August, 1947). Previous experiments to determine its action, toxicity and antihistamine properties were sufficiently encouraging to warrant its use in treatment of certain allergic and some other dermatoses.

In the clinical studies thephorin was used to treat serum sickness, dermographism, urticaria, and allergic eczema and other dermatoses. It was effective in treating 33 of 41 patients with dermatoses characterized by wheal formation. Thephorin was a worthy adjuvant in allaying itching in 22 of 39 patients with intensely pruritic dermatoses. It was further noted that thephorin prevented itching in wheals produced experimentally.

The dosage depends on the severity of the allergic complaint and the patient's response. From one to six thephorin tablets a day (or two to twelve teaspoonfuls of thephorin syrup) will be adequate in most cases.

Chemically, this new antihistamine compound is (2-methyl-9-phenyl-2,3,4,9-tetrahydro-1-pyridindine hydrogen tartrate.

Research using thephorin was carried on by the department of Dermatology, College of Physicians and Surgeons, Columbia University, New York.

**DEXEDRENE SULFATE ELIXIR** . . . furnishes a highly palatable preparation of the central nervous stimulant dexedrene sulfate. Dexedrene sulfate elixir is therapeutically identical with the tablets, and the indications are also similar. Each 5 cc. (one teaspoonful) of the elixir supplies 5 mg. of dextro amphetamine sulfate. It is available in 6 fluid ounce bottles from Smith, Kline and French Laboratories.

**BENZEDRENE SULFATE CAPSULES** . . . which provide a new oral dosage form of benzedrene sulfate, has been released by Smith, Kline and French Laboratories. These capsules are used in conditions similar to those indicated for the tablets and elixir, such as: depressive states, narcolepsy, as an adjunct in the treatment of alcoholism, and in postencephalitic parkinsonism. Each benzedrene sulfate capsule contains 5 mg. of racemic amphetamine sulfate and is available in bottles of 50 capsules.

## GADGET SHOW

Tentative plans for the third Institute on Hospital Pharmacy to be held on the East Coast this spring, call for a "Gadget Show". This will be an exhibit of photographs, lantern slides, or actual equipment "home-made" by the pharmacist (or hospital maintenance crew). Such equipment can be considered as any time-saving apparatus that is not presently available for purchase and which, because of that fact, was planned and made in the hospital for use in the pharmacy.

All persons possessing such equipment should feel the obligation to display it, so that hospital pharmacists in general may benefit. Full information for exhibiting "gadgets" can be obtained from Herbert L. Flack, Chief Pharmacist, Jefferson Medical College Hospital, Philadelphia 7, Pennsylvania.

It is thought that every hospital pharmacist has at least one gadget, which makes a possible three thousand or so gadgets for display. Only by cooperation of every hospital pharmacist, will there be any value in this Swapping Session.

EDITED BY  
HERBERT L. FLACK, CHIEF PHARMACIST  
JEFFERSON MEDICAL COLLEGE HOSPITAL, PHILADELPHIA

## THE HOSPITAL PROGRAM - U.S.P.H.S.

The Hospital Survey and Construction Act, which became law in August 1946, has launched the most comprehensive program in the history of this country for the construction of hospitals and health facilities. To help communities realize the benefits of this legislation, the U.S. Public Health Service has recently issued a series of five pamphlets:

**THE HOSPITAL SURVEY AND CONSTRUCTION ACT** is a summary of the law and regulations.

**WHY WE NEED MORE HOSPITALS** gives the story of hospital needs in this country.

**THE HOSPITAL ACT AND YOUR COMMUNITY** tells in simple terms what the program means to states and communities.

**HOSPITAL QUIZ** is a series of questions and answers on hospital planning.

**WHAT IS A HOSPITAL SYSTEM?** describes a coordinated hospital system, intended to extend the scope of hospital care.

Sample copies of these pamphlets are available free on request to the U. S. Public Health Service, Washington 25, D. C. Every hospital pharmacist should have a basic knowledge of the purpose and provisions of this act. The material included in these pamphlets presents the facts very concisely.

It is interesting to note that although hospitals are about the sixth largest type of business in the United States, it is estimated that more than 900,000 additional beds are needed. These are required to increase hospital facilities to something near "adequate" as defined by this Act. It has been estimated by authorities working under provisions of the Act, that we should have at least 4.5 general hospital beds per thousand pop-

ulation; we have about 3.5 per thousand, not counting beds in Federal hospitals which do not serve the general public. It is a sad commentary that authorities estimate to provide adequate facilities, we need mental hospitals in the ratio of five beds per thousand population, a figure larger than that for general hospital needs.

Interesting facts about hospital needs are as follows (excerpted from the aforementioned pamphlets):

1 - No state has as many general, mental, and tuberculosis beds as it needs.

2 - More than 40% of all the counties in the United States, with a total population of 15,000,000 have no registered general hospitals at all.

3 - Surveys have indicated that one general hospital out of four is not acceptable by today's standards.

4 - In all categories of hospitals, more than 900,000 additional beds are needed to provide adequate service.

5 - If all monies are appropriated under this Act, and matched by the various states, the total amount available for hospital construction during the five years will be \$1,125,000,000.

6 - It is desirable that general hospitals range in size from 50 to 700 beds. Hospitals of over 700 beds tend to lose personal relations in their services. On the other hand, hospitals of less than 50 beds, generally cannot afford to provide the varied types of service needed.

7 - Total cost of construction and equipping a new hospital will vary in different parts of the country from \$8,000 to \$12,000 per bed.

8 - In general, it takes 1.5 persons per patient per day to operate a hospital efficiently.

The estimate for general hospitals of 250,000 additional beds needed, presents a challenge to hospital pharmacy. It is accepted that for efficient operation of a hospital pharmacy, in a general hospital, one pharmacist is required per hundred beds. This means, that on top of present personnel requirements for hospital pharmacists - which are not being adequately met, an additional 2500 trained hospital pharmacists will be needed in the near future to accommodate the required expansion of general hospital facilities. These do not include needs for tuberculosis,

To make this section of value, readers must cooperate by sending news to Mr. Flack. Legislation affecting hospital pharmacy, hospital pharmacist appointments to the Boards of Pharmacy or Boards of Health, or any information which affects pharmacy and that would be of interest, is required to make this section valuable.

mental, and chronic disease hospitals and public health centers, which will require an additional 650,000 beds. Based on an estimated need of one pharmacist per 200 beds in these specialized institutions, an additional 3250 trained hospital pharmacists will be required for this group.

#### U.S.P. XIII SUPPLEMENT

The first U.S.P. XIII Sheet Supplement has been published recently. It may be obtained by sending a post card to: U. S. Pharmacopoeia, 4738 Kingsessing Avenue, Philadelphia 43, Pennsylvania.

#### PLANS OF GENERAL HOSPITALS - U.S.P.H.S.

In the January 1948 HOSPITALS, the Division of Hospital Facilities, U. S. Public Health Service presents Plans of General Hospitals for the Co-ordinated Hospital System. Hospital pharmacists might well obtain this issue and cut out and file this section for future reference.

#### THE HOSPITAL PHARMACY EQUIPMENT AND SUPPLY LIST - U.S.P.H.S.

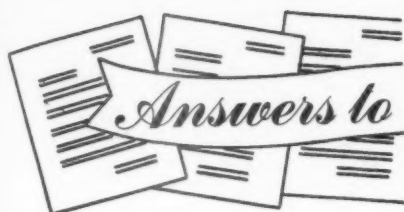
The U. S. Public Health Services Division of Hospital Facilities has presented a noteworthy contribution to the literature of hospital Pharmacy in a booklet entitled "The Hospital Pharmacy Equipment and Supply Lists", a copy of which was mailed to every member of the American Society of Hospital Pharmacists in January.

In the letter which accompanied this booklet, Doctor McGibony, Assistant Chief of the Division of Hospital Facilities, requested our "full cooperation in efforts to promote this phase (Pharmacy) of hospital services. We will appreciate any comments, criticisms, or suggestions that you might have as to how we may improve our methods of assisting the States, communities, and individual hospitals" (in the construction program).

Here is a challenge to every hospital pharmacist to read critically the twenty-two pages of this pamphlet and, if he feels that certain changes should be made, to communicate with Dr. McGibony's office and express this criticism. Unless organized hospital pharmacy cooperates with such requests, it cannot hope to obtain ideal hospital pharmacies staffed by competent hospital pharmacists.

SIZE OF GENERAL HOSPITAL - BEDS	SIZE OF PHARMACY (APPROXIMATE)	LOCATION
30	8 x 18 feet (Drug Room)	Near Clinic entrance
40	11 x 16 feet (Drug Room)	Inside main entrance
50	8 x 14 feet (Drug Room)	1st floor O.P.D. waiting room
75	12 x 18 feet (Drug Room)	Opposite O.P.D. waiting room
100	14 x 20 feet (Pharmacy) 10 x 20 feet (Solution Room) (480 square feet - total)	1st floor inside O.P.D. entrance. (Adjacent rooms)
150	14 x 20 feet (Storage) 8 x 10 feet (Drug Dispensary) 12 x 20 feet (Dispensing) 8 x 20 feet (Manufacturing) 8 x 20 feet (Solutions) (920 square feet - total)	Ground floor 1st floor, O.P.D. waiting room 2nd floor (adjoining rooms) (Dumb waiter runs through, connecting all floors)
200	12 x 20 feet (Storage) 16 x 20 feet (Pharmacy) 13 x 20 feet (Manufacturing) 10 x 20 feet (Solutions) (1020 square feet - total)	Ground floor Second floor (Adjacent rooms)





EDITED BY EVELYN GRAY SCOTT, CHIEF PHARMACIST,  
ST. LUKE'S HOSPITAL, CLEVELAND

### PHARMACY COMMITTEE

M. T. L. of Pa., inquires as to how an active Pharmacy Committee functions.

This subject is well covered by an article entitled, "How The Pharmacy Committee Can Aid", by R. W. Marquand, which was published in Hospitals, April, 1946, page 64. Hospitals is the official journal of the American Hospital Association. This article, as one of a group on "The Hospital Pharmacy", was reprinted by the American Hospital Association and presented to all members of the American Society of Hospital Pharmacists.

### PLANS FOR HOSPITAL PHARMACIES

S. J. of Nebraska, wants to obtain some information on a plan for a hospital pharmacy which would include manufacturing, both sterile and non-sterile.

In the same group of papers mentioned above is one by S. W. Morrison entitled "Put the Pharmacy in a Central Location". With the discussion as to what should be considered in planning the pharmacy, diagrams are included to illustrate the points. The article appeared originally in Hospitals page 57, April, 1947.

Recently the Division of Hospital Facilities, United States Public Health Service compiled a bulletin "The Hospital Pharmacy" which includes a discussion on Physical Facilities. This bulletin was sent to the members of the American Society of Hospital Pharmacists, but possibly copies could be obtained by writing to the Federal Security Agency.

### SUCROSE OCTAACETATE

D. H. of Ohio wants to know where to obtain Sucrose Octaacetate for use in Rubbing Alcohol Compound.

Sucrose Octaacetate may be obtained from Eastman Kodak Co., Organic Chemical Sales Division, Rochester 4, New York.

In the "Handbook of Chemistry" by Lange, published by Handbook Publishers, Sandusky, Ohio, on page 1522 is listed the U.S. Government formula (#23 G) which uses sucrose octaacetate as a denaturant. In this formula the finished product will contain 86.05% of ethyl alcohol by volume or 80.71% by weight.

Ethyl alcohol (190 degrees proof)	100 gallons
Acetone	10 gallons
Sucrose octaacetate	4.25 pounds

### PECTIN

G. S. of New Jersey wants to buy Pectin that may be used for oral preparations.

Pectin, N.F. VII may be obtained from the California Fruit Growers Exchange, Products Dept., Ontario, California.

### I. M. QUINIDINE

R. L. of Ohio, inquires as to a source of Quinidine HCl ampuls for intramuscular use.

I do not know a commercial source of the hydrochloride salt but a small number of 10 cc. ampules of Quinidine Lactate with 0.65 grams per ampul may be obtained for experimental use by cardiologists if they write directly to Dr. Kenneth Kohlstaedt, Medical Department, Eli Lilly and Company, Indianapolis, Indiana.

In the Journal of the American Medical Association, March 20, 1943, Volume 121, #12, page 917 there is an article by Drs. Sturnick, Riseman, and Sagall, on intramuscular quinidine in cardiac arrhythmias. The included formula is

Quinidine Hydrochloride	15 Grams
Antipyrine	15 Grams

Urea 20 Grams  
Distilled Water, to make 100 cc

The authors say, "No difficulty was encountered in making this solution" . . . "The mixture results in a clear colorless solution with 0.15 Gm. of quinidine hydrochloride in each cubic centimeter. Sterilization is best carried out by passage through a Berkfeld filter, after which the solution can be stored in ampuls or rubber stoppered bottles available for emergency use. After several months this solution, like all quinidine solutions turns brown, . . . but is not accompanied by any discernible change of potency or by adverse reactions". In a note Mr. Harry Brass, Ph.G. was given credit for helping in the preparation of the injection.

#### PARCHMENT PAPER AND CELLOPHANE

M. I. of California, wishes to know where he may purchase parchment paper and cellophane suitable for use in covering containers for sterile solutions.

Parchment paper under the name of "Patapar" (#27) may be obtained from the Paterson Parchment Paper Co., Bristol, Pa.

Cellophane #300 P.T. not waterproof is manufactured by Dupont and may be obtained from H. D. Catty Corp., 68 W. Huron Street, Buffalo, New York. They will cut it into the desired size. By inquiring directly to E. I. du Pont de Nemours and Co., Wilmington, Delaware, a jobber nearer any particular locality could be obtained.

#### USE ETHER OR ETHYL OXIDE

H. F. of Pa., inquires if it is necessary to use Ether U.S.P. XIII for the preparation of a rectal anesthesia or if U.S.P. Ethyl Oxide could be used.

This brings up the old question of bulk ether for use in anesthesia. For a long time ether was thought to oxidize to impurities such as aldehydes and peroxides, in a very short time, unless stored in a small special container and used quickly after opening. The aldehydes and peroxides are considered to be local irritants and so could be irritants to the lining of the colon as well as to the lungs. Some years ago considerable publicity was given to the subject of bulk ether in anesthesia in such articles as,

- 1) An Editorial - "The Use of Bulk Ether in Anesthesia" in the A.M.A. Journal for Sept. 5, 1942, page 49.

- 2) Gold, Harry: "The Use of Bulk Ether in Anesthesia," in A.M.A. Journal for Sept. 5, 1942, page 44.
- 3) "Handling Ether in Hospitals," National Board of Fire Underwriters, Bulletin 115, January 2, 1941.
- 4) Clarke, Donald: "Technique for Preparing Bulk Anesthesia Ether," American Professional Pharmacist, February, 1942.
- 5) Bourne, Wesley: "Pure Ether and Impurities," A review from Anesthesiology, Vol. 7, No. 6, November, 1946.

Ether, under the prescribed conditions of packaging, testing and use, does not deteriorate as formerly thought, but this change in thought is evidenced by the Ether for Anesthesia, U.S.P. XIII which allows 3 Kg. packages, and even larger for shipping if repackaged as directed. The U.S.P. lists an Ethyl Oxide for solvent ether which appears to require that it meets all the requirements except in the aldehyde tests for Anesthesia Ether.

Since the U.S.P. has expanded its requirements for Ether, it would seem better, at present, to avoid censure by not using Ethyl Oxide unless one could run all necessary tests to show the two to be identical.

#### VOLATILE DEODORANT

E. B. M. of Columbus, Ohio, wants a formula for a deodorant to be used with a wick for use in a hospital.

The following formula may be used by means of a dispenser such as an alcohol lamp. When needed the dispenser is placed under the patient's bed and by removing the cover from the wick the solution will slowly evaporate. When not in use the wick should be kept covered.

Neutroleum Alpha	5%
Alcohol (isopropyl or ethyl)	50%
Wetting agent	0.5%
Distilled Water to make	100%

Sodium Lauryl sulfate is a suitable wetting agent and may be obtained from E. I. du Pont de Nemours and Co., under the trade name of Duponol C or a similar type of wetting agent would be the household product Dreft. Neutroleum Alpha is a product of Fritzche Brothers, Inc. 76 Ninth Ave., New York 11, New York.

# NOTES AND SUGGESTIONS

EDITED BY

GEORGE L. PHILLIPS

ASSISTANT CHIEF PHARMACIST  
UNIVERSITY HOSPITAL, ANN ARBOR, MICHIGAN

## TOCOPHEROLS AS ANTIOXIDANTS FOR VITAMIN A

The addition of 0.1% beta or gamma tocopherol (vitamin E) will serve as a preservative or antioxidant in vitamin A preparations. Alpha tocopherol is not effective. Lecithin at a 1% concentration further enhanced the preserving qualities of the tocopherols. Reference: Ind. & Chem. Eng. 39:224, 1947.

## ALCOHOL SHORTAGE

An interesting article on the reasons for the shortage and current high price of alcohol appears in the Nov., 1947 issue of Drug and Cosmetic Industry. Shortage and high price of the precursor, molasses, is given as the chief blame.

## PHENYLMERCURIC COMPOUNDS

The phenylmercuric salts have proven their usefulness around the hospital as an extremely potent chemical suited for inclusion in germicidal solutions. A booklet containing valuable information on properties and uses of the phenylmercuric compounds is available on request from: The Edeval Laboratories, Inc., 732 Federal St., Chicago 5, Ill.; and from Metalsalts, Inc., 200 Wagarow Road, Hawthorne, N. Y.

## ALUMINUM HYDROXIDE GEL

A booklet has been prepared containing information on aluminum hydroxide gels together with data concerning preparation of the gel from a concentrated compressed paste of aluminum hydroxide.

The booklet may be obtained by writing to: Reheis Co., Inc., 88 Shipman St., Newark 2, N.J.

## PROTECTIVE SKIN CREAMS AND LOTIONS

For excessive dryness and chapping of the skin, the following formulations are useful:

### Lotion

Tragacanth, powdered	1.0 gm.
Alcohol	7.0 cc.
Glycerin	14.0 cc.
Peanut Oil	3.5 cc.
Tincture of Benzoin	2.0 cc.
Distilled Water, to make	100.0 cc.

This preparation does not leave the skin greasy and is satisfactory when applied to the skin after washing. For large area coverage a soft, easily spreadable cream or ointment has been suggested according to the following formulation:

### Cream

Peanut Oil	20.0 cc.
Hydrous Wool Fat	20.0 gm.
Petrolatum	60.0 gm.

If the lesions are moist a zinc paste similar to the following may be useful:

Kaolin	18.0 gm.
Zinc Oxide	25.0 gm.
Liquid Petrolatum	7.0 cc.
Hydrous Wool Fat	25.0 gm.
Petrolatum	25.0 gm.

Simple Ointment B.P. or U.S.P. is also suitable for dry patches of skin or for protecting the skin surrounding boils and infected areas from pus.

References: The Practitioner (British) May (1946) p. 362; The Pharmaceutical Journal, June 1, 1946.



### SWEAT RESPONSE TEST

The hospital pharmacist will occasionally be asked to furnish the necessary materials to perform the diagnostic sweat response test. The test may be employed for the diagnosis and classification of injuries to a plexus or peripheral nerve and to the individual parts of the sympathetic nervous system and spinal cord. The test has numerous uses, one of which is the investigation of the effects of drugs on sweat secretion. It may also be used to investigate endocrine and dermatological problems.

#### Iodine and Starch Method

The iodine solution is painted onto the skin of the area to be tested and allowed to dry, after which a light dusting of dry starch powder is applied. Stimulatory procedures such as exercise, etc. are then carried out and if sweating occurs the iodine is wet and forms the characteristic blue color of starch iodide. The formula for the iodine solution employed is as follows:

Iodine Crystals	1.5 gm.
Castor Oil	10.0 cc.
Absolute Alcohol, to make	100.0 cc.

The starch may be dried in the oven if necessary.

#### Quinizarin Compound

This is a patented preparation for studying sweat response prepared by Burroughs Wellcome and Co. This compound is a mixture of 28 per cent 2:6 disulphonic acid with sodium carbonate and maize starch. The powder is grayish in color and is dusted over the area to be examined by means of a small pad of cloth using moderate pressure to insure penetration of the orifices of the sweat ducts. If sweating occurs the skin becomes a bluish violet color and the sweat duct outlets appear as minute dark dots contrasting with the dry areas which remain light in color. The color contrasts can be photographed. Reference: British Pharmaceutical Journal, May 31, 1947, p. 375.

## A Method for Making Lantern Slides\*

HANS NEUBERGER

*Division of Meteorology,  
The Pennsylvania State College*

Professional workers often have the problem of preparing illustrations for a lecture to a lay or technical audience. The decision regarding the number of lantern slides to be used rests frequently upon three factors: (a) the available funds, a consideration rarely negligible at academic institutions, particularly when slides are to be shown on a single occasion; (b) facilities for preparation of reproducible drawings; (c) the availability of prompt photographic service (capable of filling last-minute orders). The end result is often a great dearth of illustrations and a crowding of information on a few slides. This latter usually leads to illegibly small print of letters or numbers.

The effective lecture appeals to the visual rather than the auditory comprehension of an audience. Particularly, the merely oral mention of numerical values or the description of conditions, arrangements, trends, etc., generally leave too much to the imagination of the listeners and tax their retentive capacity to such an extent that they find it difficult to follow subsequent statements or reasoning. Therefore, the generous employment of lantern slides is highly desirable. In most cases, it is not necessary to exhibit masterpieces of draftsmanship. Legibly printed words or numbers, schematic sketches of diagrams, and even cartoons serve in good stead.

The author happened upon a direct method of making slides which eliminates the expensive photographic process and may be useful to others.

Typing on cellophane, with an inverted sheet of carbon paper on the back side for increased density of the print, is probably a well-known expedient. The results of this method are, however, often disappointing because of unwanted carbon adhering to the cellophane or because of smudges from the typewriter ribbon. Also, cellophane does not offer a good drawing surface.

A more versatile and convenient material for making slides is available in "Permafilm (dull),"<sup>1</sup> a cellulose acetate with a dull finish on one side and an adhesive on the other. When this film is smoothly applied to a slide cover glass, it exhibits a high transparency and facilitates the writing, drawing, or copying of diagrams onto the slide.

While India ink is the most efficient medium for writing and drawing, ordinary pen and ink, soft pencil, or carbon pencil will also give very satisfactory results. All of these media can easily be erased or wiped off with a piece of moist-tissue paper. After the desired information has been put on the slide, a mask and another cover glass is placed on top and binding tape applied as usual. Heat from the projector lamp apparently does not affect the film even during prolonged exposure.

<sup>1</sup> Formerly "Dulseal," by Denoyer-Geppert Company, Chicago, Illinois.

\*SCIENCE, January 2, 1948

## The Antibiotics

### DOSAGE SCHEDULE OF PENICILLIN

Marshall, E. K., Jr.: The Dosage Schedule of Penicillin, Antibiotics Study Section Seminar, Bethesda, (Oct. 1) 1947.

From in vitro and in vivo experiments discussed by the author it appears that there is a persistent antibiotic effect of penicillin long after its disappearance from the blood. It appears probable that the maintenance of a more or less constant blood concentration is unnecessary for efficient therapy in the humans. This means that it should be possible to accomplish satisfactory therapy with aqueous penicillin given in 3, 2, or even 1 injection per day. Probably very little increase in total daily dosage would be necessary. Whether or not such dosage schedules can be used in all infections must be determined by careful, controlled clinical trials. In several clinics penicillin has been used successfully in aqueous solution with only 2 or 3 injections per day. This is in agreement with the argument presented above.

### TYROTHRINICIN AND SCABIES

Robinson, H. M., Jr., and Robinson, H. M.: A Newer Treatment for Scabies, South. Med. Jour., 40:1010, (Dec.) 1947.

A preparation recommended in the treatment of scabies complicated by secondary coccogenous infection in children or adults consists of the following formula:

Tyrothricin	0.05%
Benzyl Benzoate	30.0 %
Benzocaine	3.0 %
23 H. Alcohol (ethyl)	65.0 %
Distilled Water and Flavoring Agents	

This preparation obviates the necessity for using more than 1 method of treatment, or more than 1 preparation.

The results of treatment of 71 cases of scabies with this benzyl benzoate-tyrothricin mixture is available. The majority of the cases were associated with a superimposed pyogenic dermatitis.

In 69 cases there were no lesions at the end of 14 days. One moderately severe reaction was encountered.

### STREPTOMYCIN IN OPHTHALMIC DISORDERS

Epstein, E.: Report on Streptomycin in several Ophthalmic Cases, South African Med. Jour., 21:793, (Oct. 25) 1947.

A case of deep choroiditis, probably tuberculous in origin, is presented. Successful results were obtained in the patient with the use of streptomycin. One gram of the drug was administered in divided doses every day for 4 weeks. Improvement was noted by the patient after one week and clinical cure was achieved at the end of 2.5 months.

A few cases of indolent infective corneal ulcers responded in 3 days to a solution containing 1 per cent of streptomycin in normal saline. The solution, used as drops, was instilled in the infected eyes every hour the first day, every 2 hours the second day, and every 4 hours on the third day.

### STREPTOMYCIN THERAPY IN TUBERCULOSIS

McDermott, W., et al.: Streptomycin in the Treatment of Tuberculosis in Humans. 1. Meningitis and Generalized Hematogenous Tuberculosis, Ann. Int. Med., 27:769, (Nov.) 1947.

The results of 17 patients with meningeal, miliary or other forms of generalized hematogenous tuberculosis treated with streptomycin are reported. In every instance there was a striking alteration in the course of the infection. Six of the 17 individuals attained complete remissions which were maintained for 5 to 12 months after the completion of therapy. Evidence of therapeutic activity was afforded by; the uniformity with which the administration of streptomycin was accompanied by marked clinical and roentgenologic improvement, the disappearance of tubercle bacilli from those discharges in which they had been easily demonstrable before therapy, and an impressive degree of healing of

the lesions in the lung as revealed by histologic examination.

Although the administration of streptomycin sometimes results in a permanent remission of infection, it may also be followed by relapse in others when the antimicrobial action is no longer exerted. In generalized hematogenous tuberculosis, the appearance of tubercle bacilli which are resistant to the action of streptomycin in vitro reflect the presence of a drug-resistant infection in vivo.

#### CARONAMIDE AUGMENTS PENICILLIN LEVELS

Loewe, Leo, Eiber, H. B., and Altire-Werber, Erna: Enhancement of Penicillin Blood Levels following Oral Administration of Caronamide, *Science*, 106:494 (Nov. 21) 1947.

Caronamide, an oral preparation, was found to help conserve the consumption of penicillin where massive daily dosages were required, by consistently enhancing penicillin levels.

In the last 15 of 150 patients with subacute bacterial endocarditis, daily doses of from 5,000,000 to 40,000,000 units of penicillin were required with or without enhancing agents. Treatment was given by continuous venoclysis for at least 8 weeks with the addition of heparin and sometimes also streptomycin. Three patients were again treatment failures, the others were cured. In some earlier cases, p-aminohippuric acid was used but technical difficulties prevented continued intravenous use of this agent. It has

been found to be ineffective when given by mouth. With 3 grams of caronamide given orally every 4 hours, it was possible to obtain considerably increased blood levels of penicillin, the minimal increase being 2-fold, the maximal 7-fold. Side effects were minor and transitory; a reducing substance was found in the urine. A table presents the data on 9 patients given combined penicillin-caronamide therapy.

#### WILL PENICILLIN REMAIN EFFECTIVE?

Editorial: The Waning Power of Penicillin, *Brit. Med. Jour.*, 2:874 (Nov. 20) 1947.

Penicillinase-producers are naturally resistant, and from very small beginnings are rapidly coming to occupy the places left vacant by their more vulnerable cousins. It is a problem not peculiar to staphylococcal infection, although more serious in relation to this than any other. The power of penicillin over grave staphylococcal infections is well on the wane. There are already abundant records to show that staphylococci, like other species, may acquire immense resistance to this antibiotic within a very short time. Streptomycin is unlikely to do more than help to bridge a short gap between penicillin and some new form of chemotherapy. The use of penicillin should be restricted to cases in which there are clear indications for it. Its indiscriminate use is a potent factor in breeding resistant strains of bacteria.

We are pleased to announce the appointment of two additional hospital pharmacists to the editorial staff of THE BULLETIN.



Mrs. Anna D. Thiel, chief pharmacist of Jackson Memorial Hospital in Miami, Florida and president of the Southeastern Hospital Pharmacists Association, was born in Maine and was graduated from the Massachusetts College of Pharmacy. Acknowledged as one of the country's outstanding hospital pharmacists, Mrs. Thiel, in addition to

her fulltime job at the hospital, has her home, her two lovely daughters, and many outside activities. As assistant editor, Mrs. Thiel will be responsible for the selection of descriptions of the organization and physical arrangement of hospital pharmacy departments.



Albert L. Picchioni, pharmacist at University Hospital, Ann Arbor, Michigan was graduated from the Montana State University School of Pharmacy with honors in 1943. He served as a pharmacist and first sergeant with a combat medical battalion in France, Belgium, Germany, Austria, and the Philippines. Mr. Picchioni will bring

you information on new drugs which are about to be, or have recently been, released for general use. He will also cite pharmaceutical and therapeutic advances in specialized fields such as the vitamins, amino acids, antibiotics, and so on.



# THE VETERANS ADMINISTRATION PHARMACIST

Rx  

39

EDITED BY EDDIE WOLFE, CHIEF PHARMACIST, MT. ALTO VETERANS HOSPITAL  
WASHINGTON, D.C.

## MEET A BRANCH PHARMACIST



Wilbur C. Anderson, a native of Pittsburgh, Pennsylvania, obtained his Ph.G in 1931 and after managing a chain store pharmacy for five years, returned to the University of Pittsburgh to obtain his B.S. degree in pharmacy in 1937 and MSc., majoring in bacteriology in 1930. He served as medical representative for a prom-

inent pharmaceutical house in Washington, D.C. before entering the Army as a private. He served at the Binghamton Medical Depot for three years and as Adjutant 38th General Hospital in Cairo, Egypt for one year. He was separated from the Army as a Major M.A.C. in 1946.

He is, at present, serving on the Membership Committee for the A.S.H.P. and is auditing the course on hospital pharmacy given by the Philadelphia College of Pharmacy and Science and Jefferson Medical School Hospital.

Mr. Anderson holds the position with the Veterans Administration as Chief of the Pharmacy Section, Medical Service, Branch Office No. 3, Philadelphia, Pennsylvania.

## V.A. BRANCH OFFICE

Branch Office 3 of the Veterans Administration is located in Philadelphia, and is responsible for the administration of veteran's affairs in Pennsylvania, New Jersey, Delaware and four counties in West Virginia. The branch area serves a veteran population of 4,140,000.

Under the jurisdiction of Branch 3 are six hospitals with a total of 6,755 available beds; five regional offices and forty-one V.A. offices which were formerly referred to as sub-regional and contact offices. Additional hospitals have been proposed for this branch area.

The professional medical and allied personnel on duty in this area is 646, (a breakdown of 84 military physicians and 98 resident physicians with 214 attending and consultant physicians.) The hospitals have affiliations with the University of Pittsburgh, Pennsylvania State College, Temple University, Jefferson Medical School and Philadelphia Women's Medical College.

There are fourteen pharmacies in this branch area in operation at this time, employing twenty-five pharmacists. Competition for the pharmacy positions has been very enthusiastic as this type of work has advantages over the present type of retail pharmacy. The forty-hour work week and security offered in government service is an added incentive. We are particularly fortunate in having five schools of pharmacy in the branch area and have been successful in obtaining men of high caliber. Ninety-five percent of our pharmacists are members of the American Pharmaceutical Association and the American Society of Hospital Pharmacists.

In addition to administering to the pharmacies in V.A. activities, this office acts as liaison between the V.A. and secretaries of the State Pharmaceutical Associations in the administration of the "hometown" pharmacy service. It is intended in the near future to have the supervision of this program centralized at branch level.

The secretaries in the tri-state area have given full cooperation in making this program a success and at present the program is functioning on a current basis in the three states.

Note: All figures are as of August 31, 1947.

## YOUR V.A. HOSPITAL

We are going to publish a series of pictures of V.A. Hospitals. This will enable pharmacists in other hospitals to familiarize themselves with the V.A. Hospital Program.

Your editor would appreciate photographs and information about your pharmacy and hospital, to be published in this column.

### DR. W. PAUL BRIGGS RESIGNS FROM THE VETERANS ADMINISTRATION



Dr. W. Paul Briggs, chief of the Veterans Administration pharmacy division, resigned his position December 24, 1947, Dr. Paul R. Hawley, VA's chief medical director, announced. Dr. Briggs returned to active duty in the U.S. Navy as a Commander on January 5, 1948.

Dr. Briggs had been with VA since March, 1946. Among his major accomplishments during his year and three-quarters of service have been the establishment of a home-town pharmacy program and the improvement of the calibre of pharmacy service in VA hospitals, homes and regional offices.

The home-town pharmacy plan was organized - with the cooperation of State Pharmaceutical Associations in 46 states and the District of Columbia - to provide drugs and medicines at local pharmacies to veterans with service-connected disabilities undergoing outpatient treatment.

The quality of pharmacy service in VA hospitals and homes was improved by advancing the professional standards for the appointment of VA pharmacists, and by redefining the scope of their duties.

Dr. Briggs, in addition, developed a procedure for the selection of drugs used in VA hospitals and homes by creating standing Committees on Therapeutic Agents in each VA field station. An Executive Committee on Therapeutic Agents was formed in the VA Central Office in Washington, D. C. - with Dr. Briggs as Secretary - to coordinate the operations of the field committees.

### GEIGER APPOINTED CHIEF OF PHARMACY DIVISION IN V.A.



E. Burns Geiger has been appointed chief of the Pharmacy Division of the Veterans Administration Department of Medicine and Surgery, according to a recent announcement by Dr. Paul B. Magnuson, VA's Chief Medical Director.

Before his new assignment, Mr. Geiger was assistant to W. Paul Briggs, former chief of

the division who resigned late in December, 1947 to return to active duty as a Commander in the U.S. Navy.

Receiving a B. S. in pharmacy from George Washington University at Washington, D. C., in 1936, Mr. Geiger operated a retail pharmacy in Hagerstown, Md., until he was commissioned in the Navy in January, 1943.

He served aboard the USS Texas and USS Iowa and was released to inactive duty in January, 1946, as a lieutenant. From January, 1946, until he joined V.A. in May of that year, he was pharmacist at the Washington County Hospital in Hagerstown.

Mr. Geiger is a member of the A.S.H.P. and participated in the 1947 convention in Milwaukee. He is also a member of the American Pharmaceutical Association and the Maryland and the District of Columbia Pharmaceutical Associations.

### GRAY SUCCEEDS BRADLEY



Carl R. Gray, Jr., veteran of both World Wars and a railroad man, became Administrator of Veterans' Affairs in a formal ceremony at the Veteran's Administration on New Year's Eve to succeed General Omar N. Bradley, who has been nominated to take over the job of Chief of Staff of the Army.

In a recent radio speech, Mr. Gray stated that he intended to continue in every possible way the policies which have governed the development of the V.A. Medical Program during the past two years.

A portion of the statement of Carl R. Gray, Jr., upon taking oath of office as Administrator of Veterans Affairs, is as follows:

"To insure the continuation of the policies which have governed the development of the medical program of the Veterans Administration during the past two years, which program I fully approve and intend to further in every possible way, my first official act is to appoint Dr. Paul R. Hawley as Special Assistant to the Administrator of Veterans Affairs. Dr. Hawley has the confidence of the medical profession. He has complete understanding of the veterans' needs. I am grateful that he has arranged his affairs so that he is available to assist me in carrying out the fine program which he has been directing."



LEBANON V.A. HOSPITAL

#### LEBANON HOSPITAL PHARMACY

Among the newer hospital pharmacies containing the latest style approved equipment, is the pharmacy in the Lebanon V.A. Hospital, Pennsylvania.

The virtues of some of the drugs stocked in the pharmacy are explained by Mr. R. R. Eschenbaugh, Chief Pharmacist to Dr. Adam G. Allen, Chief, Professional Services and the Manager, Dr. W. J. McCarthy.



The above photograph is the Lebanon V.A. Hospital, Lebanon, Pennsylvania; the pharmacy is located on the first floor, convenient to outpatient clinics and other departments.

Left to right, Dr. W. J. McCarthy, Manager, Dr. A. G. Allen, Chief Professional Services, R. R. Eschenbaugh, Chief Pharmacist at Lebanon V.A. Hospital.



VA HOSPITAL, WACO, TEXAS



VA HOSPITAL, BAY PINES, FLORIDA



VA HOSPITAL, JEFFERSON BARRACKS, MO.



# SOUTHEASTERN HOSPITAL

## PHARMACY ASSOCIATION



Standing Mrs. Thiel, President of SEHPA left to right, Paul Rees, Albert Lauve, Mrs. Thiel, Gloria Niemeyer, Charles Wilson.



Speakers Thompson, Bowles, Gaines, McLusky, Falkenberg, Thiel, Rees, Millis, Niemeyer, Wilson, Lauve, Vance.



Speakers table, Falkenberg, Millis, McLusky, Rees, Lauve, Thiel, Niemeyer, Wilson, Vance, Evans.

Forty-one enthusiastic pharmacists from seven states convened in Atlanta January 17 and 18 as the Southeastern Hospital Pharmacy Association held its second semi-annual meeting at the Piedmont Hotel. Ten papers, all thought-provoking and informative, were read by outstanding men in the field both sectionally and nationally. The program included a field trip through the Emory University Hospital. Over one hundred hospital pharmacists, pharmaceutical representatives and their guests attended the evening dinner January 17.

Paul T. Rees, Special Representative, Bristol Laboratories, Washington, D. C., spoke on "The National Whole Blood Program as Intended by the American Red Cross." Mr. Rees, a leader in blood research for the Navy during the war, outlined the colorful history of the wartime program of the American Red Cross which cost \$15,870,000 or about \$1.19 per pint of blood.

In June 1947, according to Mr. Rees, the Board of Governors of the American Red Cross decided to institute a national peacetime whole blood program. This decision came after consultation with the American Medical Association and the Association of State and Territorial Health.

"There is a definite place for pharmacy, particularly hospital pharmacy, in this blood program," the speaker said, "but the pharmacists must recognize it and make a niche for themselves." It was pointed out that in areas where no hospitals were located, but where pharmacists were available, the pharmacists would be the logical persons to administer the program. In addition, small hospitals with no laboratories and no complete pharmacies which were served by one part-time pharmacist, might logically place the blood program in the hands of the pharmacist.

Guy Trimble, a national representative in the U.S. Public Health Service, himself a pharmacist, outlined the place for hospital pharmacy in the building program now under way which is sponsored by the Hospital Survey and Construction Act. Present plans call for a full-fledged pharmacy in all such hospitals over 100-bed capacity. Those hospitals which are to have under 100 beds will have a drug room where simple compounding may be done. Mr. Trimble emphasized, however, that while pharmacy was well represented in the national planning done under the Hill-Burton Act Authority, it would remain for the pharmacists at the local levels to see to it that these national plans were actuated. To prove his contention that the pharmacy was a major consideration in this construction program, Mr. Trimble pointed to the recent release of a pamphlet titled "The Hospital Pharmacy Equipment and Supply Lists," which has been mailed to every member of the American Society of Hospital Pharmacists. This was made possible through cooperation of the Division of Hospital Pharmacy of the American Pharmaceutical Association and the United States Public Health Service, Division of Hospital Facilities. "This pharmacy pamphlet is the first of a series to be compiled on the adjunct services of the hospital," Mr. Trimble said.

"Manufacturing In a Private Hospital," a brilliant paper given by John Thompson, chief pharmacist at Touro Infirmary, New Orleans was a concise delineation of the practical possibilities for manufacturing by hospital pharmacists. For its practical applicability and progressiveness, Mr. Thompson's paper was outstanding. It will appear in a later edition of THE BULLETIN of the American Society of Hospital Pharmacists.

## Semi-Annual Meeting

By JOE VANCE SEHPA

Gloria Niemeyer, associate editor of **THE BULLETIN**, outlined the goals being sought by the American Society of Hospital Pharmacists through cooperation with the A. Ph. A.'s Division of Hospital Pharmacy.

Grover C. Bowles, of the University of Tennessee School of Pharmacy, presented a thorough paper on "Hospital Pharmacy Internships." Mr. Bowles' paper presented a clear picture of this much-debated question.

Other papers of interest were: "Relationship of Hospital Pharmacy and the Medical Profession in Community Life," by Charles E. Wilson, Corinth, Miss.; "Publicity and Its Importance in Pharmacy" by Joe Vance, South Highlands Infirmary, Birmingham, Ala.; "Functions of the Veterans Administration" by Archie Millis, Atlanta; "The Relationship of the Superintendent and the Pharmacist" by D. O. McClusky, Jr., Tuscaloosa, Ala.; and "A History of Hospital Pharmacy Progress" by Albert Lauve, New Orleans.

Plans were formulated for the annual meeting of the group in Biloxi, Miss., April 22, 23, and 24, by Albert Lauve, program chairman and Anna D. Thiel, president of the association. Joe Vance was selected to represent Hospital Pharmacy on the general program of the Hospital Conference which will be in session at this time. A nominating committee was appointed for the annual meeting. Mrs. Martha Cofield, Atlanta; Valerie Armbruster, New Orleans, and Mrs. M. Gianatelli, Mobile, were named to the committee.

Joyce Gaines, Atlanta, was chairman of the local arrangements committee, which produced this successful meeting. She was assisted by Lillian Price, Emory University Hospital; Charles T. Harrell, Wm. S. Merrell Co.; and valuable aid was given by representatives of the Upjohn Co. and the Hoffman-La Roche Co. The tour to Emory University Hospital was arranged by Hoffman-La Roche, and a breakfast by the Upjohn Co.

Officers of the association are Anna D. Thiel, president; Albert P. Lauve, vice-president; Alberta Evans, secretary-treasurer; and Joyce Gaines, president-elect.

The following members were present at this meeting: Frank Bogart, Chattanooga, Tenn.; Charles B. Barnett, Jacksonville, Fla.; Alberta B. Evans, Orlando, Fla.; Albert P. Lauve, New Orleans; Anna D. Thiel, Miami; Grover C. Bowles, Jr., Memphis; Mrs. Grover Bowles, Jr., Memphis, Tenn.; John F. Thompson, New Orleans; Valerie Armbruster, New Orleans; Lillian Price, Emory, Ga.; Leo J. Babin, New Orleans; D. O. McClusky, Jr., Tuscaloosa, Ala.; C. Joe Vance, Birmingham, Ala.; E. W. Rollins, Winston Salem, N. C.; Martha Cofield, Atlanta, Ga.; Johnnie M. Crotwell, Tuscaloosa, Ala.; Dora Gianatelli, Mobile, Ala.; Ronald A. Shumway, Atlanta, Ga.; W. D. Strother, Athens, Ga.; Charles E. Wilson, Corinth, Miss.

Visitors included: Mrs. Leo Babin, New Orleans; Lollie M. Dempsey, Athens, Ga.; Archie E. Millis, Atlanta, Ga.; W. G. Fowler, Atlanta, Ga.; W. H. Martin, Atlanta, Ga.; Guy Trimble, Washington, D. C.; Betty Little, Atlanta, Ga.; Dan E. Murphree, Atlanta, Ga.; Mrs. Lila C. Gross, Marietta, Ga.; Evelyn Snider Canterbury, Atlanta, Ga.; Charles Harrell, Atlanta, Ga.; Carl G. Knox, Atlanta, Ga.; C. H. Bishop, Atlanta, Ga.; J. A. Raudonis, Atlanta, Ga.; Charles Dillon, Cincinnati; Paul Rees, Washington, D. C.; June Snoddy, Emory, Ga.; Gloria Niemeyer, Washington, D. C.; Vivian Cato, Atlanta; Martha Cofield, Atlanta.



Gloria Niemeyer



SEHPA Officers, Joyce Gaines, Anna Thiel, Alberta Evans, Albert Lauve.



Joe Vance



Albert Lauve



Archie Millis



## CURRENT LITERATURE

### HOSPITAL MANAGEMENT

November, 1947 - "Why U.S.P.H.S. Organized a Pharmacy Service for its Hospital Division" by George F. Archambault, Chief, Pharmacy Service, Hospital Division, U. S. Public Health Service, Washington, D. C. From a paper presented before the A.S.H.P. annual meeting in 1947, - A discussion of the function, purpose, projects under consideration and possibilities for advancement in the newly created pharmacy service throughout the Marine Hospital System. page 84

"Distribute Vaccine Preventing Common Types of Pneumonia", Announcement by the Biological Laboratories of E. R. Squibb & Sons of a vaccine which makes possible the prevention of the most common types of pneumonia. A single subcutaneous injection of this immunizing agent, known as Solution of Pneumococcus Polysaccharides (Type-Specific) builds resistance to the most prevalent types of pneumococcal or lobar pneumonia. Immunity usually develops within two weeks and is effective for at least one year. page 88

"Pharmacist, Superintendent, Chief Buyers of Hospital Drugs" Report on a recent survey conducted by "Hospital Management" in reference to: persons involved in the purchase of drugs, adequacy of space allotted to the hospital pharmacy, and pharmaceutical equipment. page 90

"Adopt New State Formulary for Use in Hospitals" - Discussion of the matters considered at the quarterly meeting of the New Jersey Hospital Association. A new state formulary recently agreed upon by a joint committee of the New Jersey Medical Society and the New Jersey Pharmaceutical Association was described by Dr. Thomas D. Rowe, dean of the Rutgers University College of Pharmacy, and editor of the formulary. Education of the interns and residents in the writing of prescriptions in hospitals will be one of the functions of the formulary, and further education of this sort will be aided by posters, each carrying four prescriptions, which all hospitals will be requested to display. page 92

December, 1947 - "Central Management of Narcotics by the Pharmacist", by Joe Vance, Chief Pharmacist and Assistant Administrator, South Highlands Infirmary, Birmingham Alabama. - Describes a simple system, tailored to meet the needs of the hospital and fitting into the legal structure of the law. Essentially, it is a centralized system, wherein the central supply room with a registered nurse in personal charge issues all narcotics to be given to patients on the floors. page 76

January, 1948 - "Glycerine's Role in the Hospital" - Why the American hospital pharmacies use an average of more than three pounds of glycerine per bed, annually. page 84

"New Pharmaceuticals for the Hospital Pharmacy" - "Hospital Management" inaugurates a new department in which it reviews new pharmaceutical preparations scheduled to make their appearance in January. page 88

"Southeastern Pharmacy Group Presents Outstanding Program" A preview of the preliminary meeting of the Southeastern Hospital Pharmacy Association at Atlanta, Georgia. page 92

### AMERICAN PROFESSIONAL PHARMACIST

December, 1947 - "Pharmacy in a Public Health Service Hospital" by Ronald G. Esson, Senior Assistant Pharmacist U. S. Public Health Service; Chief Pharmacist, U. S. Marine Hospital, Seattle, Washington. - This article illustrates a typical Public Health Service installation of a Pharmacy Department. page 1112

"The DRUG ROOM" - An editorial on the impropriety of referring to the "Hospital Pharmacy" as the drug room. page 1119

### SOUTHERN HOSPITALS

December, 1947 - "With the Hospital Pharmacists", edited by Joe Vance, South Highlands Hospital. - Continued on page 46





## ORGANIZATION NEWS



**THE SOCIETY OF HOSPITAL PHARMACISTS OF GREATER CINCINNATI** has completed plans for affiliation with the national society and the necessary information has been forwarded to the secretary of the A.S.H.P.

A meeting of the Cincinnati chapter was held on January 7 at Dunham Hospital with Mr. William Herman, chief pharmacist as host. Members of the society agreed to give maximum support to the committee on legislation relative to securing better laws and requirements for hospital pharmacies and pharmacists. The membership committee urged concentrated effort by all to obtain maximum attendance at their meetings. The Cincinnati Academy of Medicine has invited representatives of the society to attend their next meeting and it is hoped that this group can foster this relationship to create a better understanding of the hospital pharmacy in this area. A film on "Modern Nutrition" was shown by Mr. John Parr, local hospital representative for the Squibb Company.

**THE HOSPITAL PHARMACISTS OF CHICAGO-LAND** held their December meeting at the Illini Union with Chairman L. G. Klemme, Elmhurst Hospital, presiding. Dr. Ralph E. Dolkart, Assistant Professor of Medicine, Northwestern University, spoke on "Clinical Aspects of Antibiotic Therapy." Dr. Dolkart discussed the results of two years' investigational work in penicillin and streptomycin therapy. He presented to the hospital pharmacists, an excellent talk which was followed by a discussion.

Officers elected to serve during the 1948 term are as follows: Chairman Louis Gdalman, St. Luke's Hospital; Vice-chairman Josephine Scalotta, Grant Hospital; Recording Secretary Sophia Poska, Loretta Hospital; Corresponding Secretary Sigrid Van Schaak, Evanston Hospital; and Treasurer John J. Spranze, West Suburban Hospital.

Chairman-elect Gdalman announced a new meeting place for the 1948 season. The Society will meet the second Tuesday of each month, at

the Chicago Hospital Council, 105 W. Adams St. at 7:30 P.M. The first meeting in 1948 will be held on January 13 at which time there will be a seminar on "Curricula in Colleges of Pharmacy - Are They Adequate?" This discussion will be directed by Professor G. Webster, Department of Chemistry, University of Illinois, College of Pharmacy and chairman of the Committee on Curriculum, American Association of Colleges of Pharmacy.

**THE HOSPITAL PHARMACISTS ASSOCIATION OF GREATER ST. LOUIS** held a meeting on January 13 at Melbourne Hotel with twenty members present. "Improving the Hospital Pharmacy and Increasing the Pharmacist's Salary" was the subject discussed by Mr. L. L. Wright of Eli Lilly & Co. Miss Ann Gestrich, pharmacist at Barnes Hospital read an article on "The Operation of an Opium Factory in China" by Rudyard Kipling. Two new members, Miss Norma Greer, pharmacist at Barnes Hospital and Mrs. Ruth Miller, pharmacist at Deaconess Hospital were accepted as new members of the Association.

**THE NEW JERSEY SOCIETY OF HOSPITAL PHARMACISTS** met at the Rutgers College of Pharmacy in Newark on December 18 at 8:30 P.M. with ten members present. Subjects discussed included the pricing of prescriptions and medications as it concerns the respective type of hospitals, and narcotic records.

**THE CLEVELAND SOCIETY OF HOSPITAL PHARMACISTS** met at Glenville Hospital, Cleveland, on Wednesday December 3. Dr. Robert W. Heinle, Assistant Professor of Medicine, Western Reserve University School of Medicine was the guest speaker. His subject was "Newer Drugs In The Treatment of Blood Diseases." He discussed the use of Radioactive Phosphorous, Nitrogen Mustard and Folic Acid. Three new mem-

bers, L. Maniaches, Cleveland City Hospital, Miss Joan Ricuitto and Miss Charlotte Cox of the University Hospitals were present.

**THE MARYLAND ASSOCIATION OF HOSPITAL PHARMACISTS** held their third annual meeting in conjunction with the Maryland-District of Columbia Hospital Association at the Lord Baltimore Hotel on the afternoon of November 11, 1947. Methods used in obtaining information for the Pharmaceutical Survey were discussed by Mr. J. Solon Mordell, Assistant Director of The Pharmaceutical Survey. Mr. Alexander M. Milne of the U.S. Public Health Service discussed the Government's plans for future hospital pharmacy facilities under the new Hospital Survey and Construction Act. Frank J. Gregorek of the Johns Hopkins Hospital demonstrated a number of time saving gadgets for hospital pharmacists. The next meeting of the Maryland Association of Hospital Pharmacists is scheduled for Saturday, January 24, 1948.

**THE SOCIETY OF HOSPITAL PHARMACISTS OF THE METROPOLITAN AREA, NEW YORK CITY**, met at the New York College of Pharmacy on Thursday, December 11 at 8 P.M. with 30 members and visitors present. Dr. Wm. Amster of the Medical Service Division of the Schering Corporation spoke on "The Use and Misuse of Hormone Products."

**THE BUFFALO CHAPTER OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS** met at the Buffalo General Hospital on December 7 at 2 P.M. Officers for 1948 were elected as follows: President Francis X. Sturner, Buffalo General Hospital; Vice-President, Edward T. Lawler; Secretary Lynn Wiles; and Treasurer Ethel Woodward.

The group was addressed by Mr. Willis D. Hall, personnel director of the Buffalo General Hospital, who has been instrumental in developing the stable relationship between the pharmacist and the administration at his hospital. An executive meeting for a later date was decided upon in order to lay plans for growth and activity of the organization this year.

**THE MICHIGAN CHAPTER OF THE AMERICAN SOCIETY OF HOSPITAL PHARMACISTS** held a dinner meeting at Henry Ford Hospital on January 8, with 75 people present. Speakers for the evening included Dr. John H. L. Watson who spoke

on "The Particles of Modern Physics" and Dr. George H. Mangum whose subject was "Some Applications of Isotopes In Medicine and Pharmacology." Mr. F. H. Taft of the State Board of Pharmacy spoke informally on the state narcotic and barbiturate law requirements. He advised hospital pharmacists to write the state board for a copy of the law if they so desire.

Mr. G. L. Phillips of the Program Committee announced that the next meeting of the Society would be February 5, 1948 at Wayne County General Hospital in Eloise and the March meeting will be held at the Holy Cross Hospital.

At the December meeting the society voted to amend the constitution and by-laws to permit "Associate" members to vote but not to hold office. Dr. Daniel J. Leithauser, St. Joseph's Hospital spoke at this meeting on the importance of restoring normal body processes in the shortest possible time after surgical procedure.

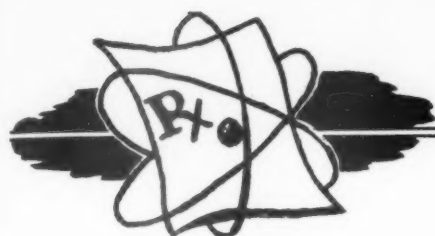
**THE MIDWEST ASSOCIATION OF SISTER PHARMACISTS** met on November 20 at 2:30 P.M. at the St. Mary of Nazareth Hospital in Chicago. There was a discussion in regard to suitable pharmacy hours in a private hospital and a film on the use of intocostin in polio was shown through the courtesy of E. R. Squibb and Sons.

#### CURRENT LITERATURE-

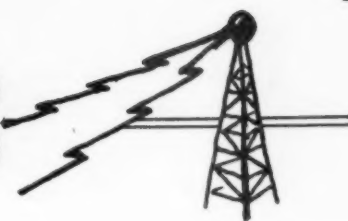
continued from page 44 -

pital, Birmingham, Alabama. - Includes the following items: "New hypnotic NU-903 Improves on Barbiturates"; Usage of Mineral Oil Comes in for Probe; Chloromysetin is Substance Effective Against Rickettsia; "Metopon and Methadon added to Morphine Group; New and Non-Official Remedies Include Eight New Drugs; Study of Hospital Pharmacy in College to be Probed; Use of word "Hospital" Prohibited in Trade Names; Louisiana Pharmacists Publish Own Bulletin; Pharmacy Article Reveals Administrators Influence; Chapter on Hospital Pharmacy Included in Text-book.

January, 1948 - "With the Hospital Pharmacists". Includes the following topics: Reactions to Penicillin Cause F.D.A. Investigation; Fishbein has Word to Say On Effects of Agerized Flour; Dissolving of Kidney Stones Accredited to Suby's Solutions; Dienestrol Is Accorded Recognition by Council; Price of Alcohol Seen Dependent on Tax - Burden; Study 'Enhancement Factor' in Amorphous Penicillin; Dye Aids in Detection of Some Cancerous Tissues; Atabrine is Now Seen to Rival Quinidine.



## NEWS ITEMS



### HOSPITAL PHARMACISTS SERVE AS OFFICERS OF A. PH. A. BRANCH

Three members of the American Society of Hospital Pharmacists have recently been installed as officers of the Northern Ohio Branch of the American Pharmaceutical Association. Mr. Clarence Miller, chief pharmacist at Glenville Hospital, Cleveland, will serve as president; Mrs. Evelyn Gray Scott, chief pharmacist at St. Luke's Hospital, Cleveland, is the new vice-president; and Russel Stimson, superintendent of Doctors Hospital is treasurer.

### JOHN DUGAN TO HEAD TAFT PHARMACY

Mr. John Dugan of New Haven, Connecticut will succeed Mr. Joseph M. Jacobs as president of the Taft Pharmacy. Mr. Dugan is a member of the A.S.H.P. and has taken an active part in professional activities of the Society and other pharmaceutical organizations.

### HOSPITAL PHARMACY REPRESENTED AT AMERICAN COLLEGE OF SURGEONS' MEETING

"More Attention Should be Given to Drug Therapy" was the subject of a paper presented by Mrs. Lillian Price before the American College of Surgeons' meeting in Atlanta, January 26 and 27. Mrs. Price is chief pharmacist at Emory University Hospital in Atlanta and has been active in the Southeastern Hospital Pharmacists' Association.

Mr. D. O. McClusky, administrator at Druid City Hospital in Tuscaloosa, presented a paper on "Increasing the Use of Hospitals". Mr. McClusky was formerly a hospital pharmacist and is a member of the A.S.H.P.

### HANSEN ADDRESSES AMERICAN COLLEGE OF SURGEONS

Mr. Hans S. Hansen, member-elect of the Council of the American Pharmaceutical Association and administrator of Grant Hospital, Chicago, spoke on January 20 to the American College of Surgeons meeting in Toledo on certain aspects of drug therapy.

Mr. Hansen will soon discuss the "Organization, Management and Functions of the Hospital Pharmacy" for the students in hospital administration at Northwestern University. The lecture will be followed by a demonstration at the Grant Hospital Pharmacy. Mr. Hansen was chairman of the A.S.H.P. in 1946-1947 and member of the Policy Committee in the Division of Hospital Pharmacy.

### HOWARD COLLEGE OFFERS COURSE IN HOSPITAL PHARMACY

Howard College of Pharmacy in Birmingham, Alabama now offers a course in hospital pharmacy which is taught by Mr. Joe Vance, assistant superintendent of the South Highlands Infirmary in Birmingham. A series of special lectures on hospital pharmacy has recently been presented by visiting lecturers. Information on the hospital use of drugs, the care and use of hypodermic syringes, the pharmacy as diabetic headquarters, the manufacture of biologicals, and the preparation and administration of intravenous solutions were presented in this series of lectures.

MR. I. WEBER, chief pharmacist of Jackson Park Hospital, Chicago has been elected to honorary membership on the medical staff.

DONALD A. CLARKE, apothecary-in-chief of The New York Hospital discussed the "Sociological Position of the Hospital Pharmacy" before Fordham College of Pharmacy Alumni at Thebaud Hall on December 10.

### DEATHS

SISTER MARY ALPHONSA, O.S.F., 71 chief pharmacist at St. Francis Hospital, Evanston, Illinois died at the hospital January 20. Sister Alphonsa was pharmacist at St. Francis Hospital for 23 years, previously following the same profession at Indianapolis, Hammond and Lafayette Hospitals. She was one of the originators of the Hospital Pharmacists Association of the Midwest and during her lifetime worked actively for her profession.



# POSITIONS in hospital pharmacy

**NEW YORK . . . WANTED**, well-trained male hospital pharmacist qualified to succeed Chief Pharmacist of 300-bed, fully approved volunteer general hospital in a Western New York city. Salary dependent upon qualifications. Address letters of application to **THE BULLETIN** of the American Society of Hospital Pharmacists, Box 222, 1313 Ann Street, Ann Arbor, Michigan.

**WASHINGTON . . . Female Pharmacists** - Single women between 21 and 40. Experienced, registered pharmacists, having a degree from an accredited school of pharmacy preferred. Applications from women who have a degree and who are presently working toward registration under direction of a qualified pharmacist will also be considered. Salaries offered will be in proportion to qualifications and experience of applicant. Address letters to Employment Office, General Electric Company, Hanford Works, Richland, Washington.

**PENNSYLVANIA . . . A position as Chief Pharmacist** is open at Reading Hospital, Reading, Pennsylvania. This is a 350-bed hospital which has plans for expansion in the near future. For further information, write to Mr. Lee Wolfe, Administrator, Reading Hospital, Reading, Pennsylvania.

## POSITION WANTED

**MISS PATTI L. CAIN**, who will receive her Master of Science degree in Hospital Pharmacy from Purdue University School of Pharmacy, Lafayette, Indiana, in June 1948, is interested in working into the position of chief pharmacist or assistant chief pharmacist in a hospital or medical center of at least 400 beds, preferably one affiliated with a medical school or university. Miss Cain is registered in Indiana and has had hospital pharmacy experience during one summer at University Hospital, Ann Arbor, Michigan and during two summers at the Indiana University Medical Center at Indianapolis. In 1945 and 1946 she was employed as pharmacist at the 450 bed Christ Hospital, Cincinnati. Miss Cain is now completing her second year of study at Purdue where she has also been an assistant in Dispensing Pharmacy. Miss Cain may be addressed at the Purdue College of Pharmacy.

## POSITION WANTED

**MR. WILLIAM H. BURKE . . . 911 Maple Avenue, Hartford, Connecticut**, desires a position as a hospital pharmacist in Southwestern United States. He has had five years experience as pharmacist in a 500-bed hospital.

## INTERNSHIPS IN PHARMACY

The Johns Hopkins Hospital, in cooperation with the Graduate School and the School of Pharmacy of the University of Maryland, announces that internships in Pharmacy will be open to a number of 1948 or other recent graduates of recognized schools of pharmacy. Appointments will be for a period of two years, beginning July 1, 1948. During this time, interns will devote one-half time to hospital pharmacy work and one-half time to graduate study. Upon satisfactory completion of the internship and the course of study, Master of Science Degrees will be conferred by the University of Maryland and Certificates of Internship will be awarded by the Johns Hopkins Hospital.

An allowance of \$100.00 per month will be provided by the Hospital, and the University of Maryland will make a reduction of 25% in tuition fees. Complete information regarding fees and curricula can be found in the catalog of the School of Pharmacy, copies of which may be secured by sending requests to the School at 32 South Greene Street, Baltimore 1, Maryland.

Interns will be required to rent rooms at the Hospital. Meals may be purchased for a nominal sum in any of several Hospital dining rooms.

Opportunity will be offered for well-rounded practical experience in hospital pharmacy administration, pharmaceutical manufacturing, dispensing, and in the preparation of sterile solutions and other sterile products. The facilities of the Welch Medical Library of the Johns Hopkins University and the library of the University of Maryland School of Pharmacy are available.

Off duty hours must be so arranged that one pharmacist intern will be on call to take care of emergency orders when the hospital pharmacy is closed. Regulations regarding personal conduct and habits will be those established by the Director of the Hospital for interns on other hospital services.

Applicants should submit a statement giving full details as to date and place of birth, citizenship, marital status, education, etc. together with a small, recent photograph. An official transcript of the applicant's college record is required. The applicant should ask the dean of his college to write to the Director giving his estimate of the applicant's personality and fitness.

Applications for appointment should be forwarded to Edwin L. Crosby, M.D., Director, the Johns Hopkins Hospital, Baltimore 5, Maryland not later than April 1, and appointments will be announced on or before May 1, 1948.